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A MANUAL

OF

GENERAL PATHOLOGY,

DESIGNED AS AN

INTRODUCTION TO THE PRACTICE OF MEDICINE.

BY

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TO

SIR JOHN SIMON, K.C.B., D.C.L., F.R.S.,

LATE MEDICAL OFFICER TO THE LOCAL GOVERNMENT BOARD: FORMERLY SURGEON TO AND LECTURER
ON GENERAL PATHOLOGY AT ST. THOMAS'S HOSPITAL,

IN RECOGNITION OF THE GREAT SERVICES WHICH BY HIS OWN

RESEARCHES, AND BY THOSE CARRIED OUT UNDER HIS

DIRECTION, HE HAS RENDERED TO THE

SCIENCE OF PATHOLOGY,

This Book.

IS RESPECTFULLY DEDICATED

BY

THE AUTHOR.

PREFACE.

THIS work is intended to provide for the use of students an introduction to general pathology, including general pathological anatomy. To draw the line strictly between these subjects and special pathology or morbid anatomy is difficult if not impossible, and it is therefore very likely that subjects have been omitted which in the opinion of some readers ought to have been included, and others have been included which may be thought to be not strictly comprised within the scope of the work. But on the whole it is thought that the various topics here treated of possess sufficient coherence to make it, at all events, convenient to study them together. In the field which it aims at covering, this book does not precisely coincide with any other now used in this country, and may thus, I hope, escape the charge of actual rivalry with the excellent text-books of pathological anatomy which we already possess. The latest text-book on the subject in English is the American translation of Uhle and Wagner's *General Pathology*, published in 1876, and with that work in respect of size and comprehensiveness the present manual challenges no comparison.

It would have been satisfactory to be able to say that the arrangement of subjects in this book is in accordance with the teaching of pathology in the London schools of medicine or in British universities. But on inquiry I have found that the methods of different teachers of pathology vary so widely that no arrangement could be framed which would have any general application. Most of the topics here treated, but not all, have at one time or another formed part of my own course; of which the scope and arrangement are not every year the same.

The only features in the book which seem to call for any special notice are the following: first, pathological histology, though not neglected, occupies a less prominent place than since the appearance of Virchow's *Cellular Pathology* it has been the custom to give it in pathological works. That an undue or at least a too exclusive importance has been attached to the forms of cells and to alterations of mere structure can hardly be denied, and it is admitted by the reaction which has set in, chiefly, perhaps, since the publication of Cohnheim's classical *Lectures on General Pathology* in 1877, in favor of a wider conception of the subject.

Secondly, an attempt has been made to do justice, partially at least, to another marked feature of modern pathology, the increased importance attached to etiology.

Although the processes of disease may be and are to a large extent studied apart from their causes, the investigation of the latter has great and independent value, which, in one department at least, I have endeavored to recognize. It will occasion no surprise that in the present state of science an important place has been assigned in the causation of disease to the influence of living and especially of vegetable organisms.

Thirdly, I must admit that greater prominence has been given to the medical than to the surgical aspects of pathology, although in truth the greater part of general pathology is not specially medical or surgical. This has been done, not only because it is with the medical side that I am most familiar, but because the surgical side has received in this country perhaps a disproportionate share of attention. The subjects commonly grouped together under the title of "Surgical Pathology" have been, therefore, in many cases somewhat lightly passed over.

Another omission which will be noticed is that there is no account of monsters and malformations. Although this subject might be rightly considered a part of general pathology, and is interesting in itself, I have found it extremely difficult to compress it into a small compass, and as it has also not much practical bearing, it seemed better in an elementary manual to omit it altogether.

Want of space and considerations of relative importance have led to the omission of other subjects not wanting in interest; but, generally speaking, a book of this size may claim to be judged rather by what it includes than by what it leaves out.

In a manual intended for students it has not been thought necessary or desirable to quote authorities as a general rule, more especially as the greater part of the facts stated are common to most European textbooks.

It is difficult in a subject which one has been for many years engaged in teaching, to say how much has been learnt from one's own experience, and how much from the writings of others; but I think I may fairly say that in structural and clinical pathology most of the statements made, except as otherwise acknowledged, are either based upon or confirmed by personal observation. It is otherwise as regards experimental pathology (with which I have no practical familiarity), and the new and highly specialized science of bacteriology. In these matters I have drawn as far as possible upon original memoirs, and carefully collated the best authorities.

Among the books to which I owe special acknowledgments are Cohnheim's *Vorlesungen über allgemeine Pathologie* and Recklinghausen's *Allgemeine Pathologie des Kreislaufs und der Ernährung*, forming a part of *Deutsche Chirurgie*. For the subject of animal parasites, large use has been made of Leuckart's classical work, recently translated into English; and for vegetable microörganisms numerous recent books and memoirs, the chief of which are mentioned in the appendix.

Of the illustrations, many are original and based upon preparations either in my own collection or in the museum of St. Thomas's Hospital (chiefly prepared by Dr. Acland), or else lent me by friends. Mainly to save expense and prevent the price of the book rising too high for its purpose, a good many blocks have been borrowed from other sources, which are duly acknowledged either in the text or in the list of illustrations.

There remains the pleasant task of acknowledging the help I have received from my colleagues and friends.

Dr. Gulliver, Mr. Anderson and Dr. W. G. Mackenzie have kindly looked over portions of the proof-sheets; Dr. Acland has not only furnished me with specimens, but superintended the execution of some of the figures; Dr. Jacob, of Leeds, and Dr. Sharkey have lent some valuable specimens; while Dr. Bristowe and Dr. Crookshank have been good enough to allow me to use some of the figures which illustrate their own works. To the Council of the Pathological Society and to Dr. Sidney Coupland I am indebted for permission to copy some figures from the Transactions of the Society.

Mr. Lapidge has been the draughtsman of most of the new figures. which have been cut on wood by Mr. Collings. Some other cuts have been executed by Mr. Daniellsen.

78 Wimpole Street, London;
April, 1888.

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EXPLANATION OF FRONTISPIECE.

RELATION OF BACTERIA TO TISSUES.

Fig. 1. Bacilli of Rhinoscleroma.

Preparation by the author. × 1000.
a, thick and thin bacilli in a lymphatic vessel.
b, nest of thick bacilli within a cell.
e, bacilli in interstitial tissue.
Methyl-violet staining by Gram's method and eosine.

Fig. 2. Bacilli of Rabbit-septicæmia within the Capillaries.

After Koch × 700.
b, bacilli; *t*, intervascular tissue.

Fig. 3. Tissue in Leprosy, showing Bacilli.

Preparation by Dr. Acland. × 700.
V, section of bloodvessel: *c*, cells containing bacilli. Fuchsine and methylene-blue staining.

Fig. 4. Tubercle-bacilli in Giant-cells, from Tubercle in the Horse.

Preparation by Dr. Acland. × 750.
a, *a*, *a*, giant-cells. Stained with fuchsine and methylene-blue.

Fig. 5. Anthrax-bacillus forming Spores. × 750.

a, rods; *b*, spores formed in the rods: *c*, spores set free.
Preparation by Dr. Acland, stained as in Figs. 3 and 4.

Fig. 6. Micrococcus tetragenus in Lung of Mouse.

Preparation by Dr. Acland. × 750.
A, alveolus: *b*, *b*, *b*, micrococci. Methyl-violet and eosine staining.

Fig. 1

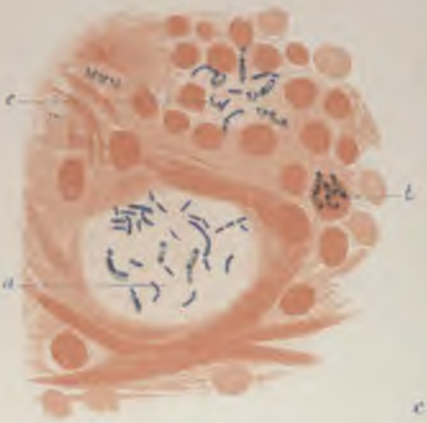


Fig. 4

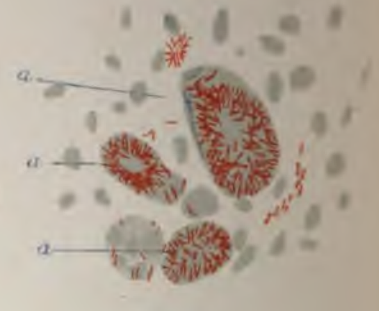


Fig. 2

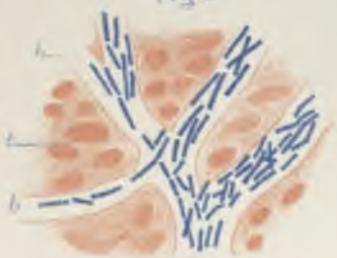


Fig. 5

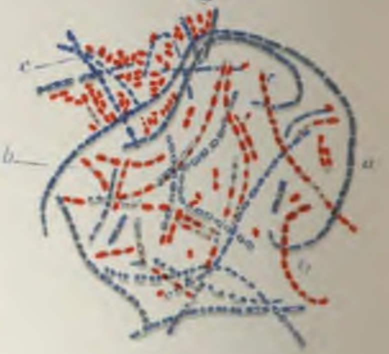


Fig. 3

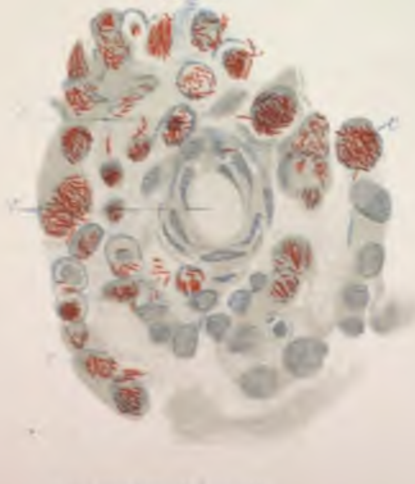
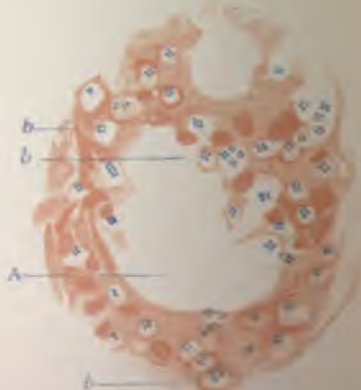


Fig. 6



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GENERAL PATHOLOGY.

PART I.

THE PROCESSES OF DISEASE.

CHAPTER I.

INTRODUCTORY.

PATHOLOGY is the science of disease—that is to say, the science which studies the human body in those conditions which it has been agreed to call diseased or morbid.

In order to define pathology it is then necessary to define disease; and in order to define disease, we must define health.

No one would willingly engage in the thankless task of definition, so especially exposed to criticism, and where success is impossible; but for the present purpose the difficulty cannot be altogether avoided.

By health, then, we understand the maintenance of a living body in such a condition that neither the performance of its ordinary functions, nor any slight disturbance of them interferes with the regular course of its activity, or leaves it worse than before.

Such a condition may be compared to one of stable equilibrium, that is, the condition of a body either at rest or in motion, such that a small disturbance does not completely alter the position of the body, but brings it back to its original position. Health is not like the equilibrium of a body at rest, for it implies life, which is a condition of incessant change. We must rather compare it to a moving equilibrium, to that of a body in uniform motion; such as a planet in its orbit, or, to take an humbler comparison, that of a spinning-top.

If we are not startled at the homeliness of this illustration, we may suppose a top thus spinning smoothly and vigorously to be analogous to a body in health. The forces which maintain it are the original movement of rotation impressed upon it, and its own weight, which gives it momentum and keeps it in due relation to the surface on which it rests. Now let the top receive a slight disturbance. The more vigorously it is spinning the less is the effect produced. But any disturbance which may result consists of a series of oscillations or movements in contrary directions, some of which directly tend to destroy the state of equilibrium, others to restore it. Each of these movements is a resultant of three forces—the original impulse of rotation; the action of gravity on the top; and the force producing the disturbance.

After a time the effect produced by the disturbance may come to an end, and the top either returns to its previous state of moving equilibrium, or else is entirely overthrown. But an irregularity of movement may, on the other hand, be set up, which may last even as long as the top continues to spin. Again, if we watch the motion of the top, we see that without any outward disturbing cause irregularities in its motion become perceptible, and tend gradually to increase. These irregularities depend upon one of these causes:

Either upon some inequality in its original construction, or in the surface on which it rests, or upon the effects of friction in producing such inequalities by wearing away the substance of the top or the surface, or else merely upon the exhaustion, by friction, of the original impulse which started its motion.

The irregularities produced by either of these causes will either bring the motion of the top to an end, or else produce such a condition of unstable equilibrium that a very slight disturbance, which before would have produced little effect, is sufficient to overthrow it.

Now, with the aid of this homely illustration, let us try to form a conception of the production of disease—that is, of deviations from health in the human body.

Let a small disturbance—that is, an injury, mechanical, chemical, physical, or from some specific cause, such as a living virus—act upon the human body. As special instances, we may call to mind the effects of such well-known agencies as a bullet-wound, a dose of corrosive poison, extreme cold, extreme heat, the contagion of some specific fever.

If the injury be slight, and the body be in a state of vigorous health, the disturbance is rapidly equilibrated, and the body returns to its normal condition. If the disturbance be greater, a series of changes is set up, which we call a disease. Some of these changes—the so-called symptoms of the disease—are destructive; others are restorative, or conservative. To the first class belong hemorrhage, fever, weakness of the heart, asphyxia, suppression of secretions, and the like. To the second class, vomiting, or diarrhœa, induced by poisons; elimination of morbid matters by the secreting organs, suppuration around the foreign body in a wound, etc., all of which tend to remove the cause of the disease and promote recovery.

It is a great mistake to suppose either that all the symptoms of disease are necessarily injurious, or that all are (in Sydenham's words) beneficent "efforts of nature to get rid of the morbific matter."

Some are of one kind, and some of the other. Of which kind each is can only be determined by observation and experiment, and only y the same means can we learn which we should attempt to ngthen, and which to suppress.

ccording as the disturbance produced by the injury is of short or long duration, we call the disease acute or chronic. It may end either in death or recovery. In the latter case either the body may return to its former state of health, or may have received some permanent damage which is likely to be the cause of disease in future.

In some cases the cause never ceases to act, and the resulting disturbance is never compensated. If, for instance, a person has received the poison of tubercle or of leprosy, it will continue to act injuriously till death results.

Let us now consider of what nature the actual disturbances produced by an injury are. They are (as in the spinning-top) the resultant of three kinds of forces: the injury, the initial impulse of life which determines growth, and the molecular forces produced by the materials of the body itself, when acted upon by all the surrounding circumstances, such as air, food, temperature, which set up in them chemical and physical changes. These are comparable to the action of gravity on a revolving body. If this be the case, it follows that the processes of disease are the same as the processes of life, *plus* an injury. We may go further and say that they are merely the processes of life differently combined, and arranged in a different order.

So that disease itself is not really anything foreign to the organism; though *causes* of disease may be, and are so.

We must not, then, think of disease as an entity, that is, of independent existence. The cause may indeed be thus regarded; and doubtless this is what is present in our minds if we say (as some do) that an enlarged liver is a disease, or a heart with imperfect valves, or a dose of sewer-gas poison, or even the acarus scabiei. It would be less incorrect (though, of course, only a metaphorical expression) to say that the disease is the body itself acting wrongly, under the influence of one of the above-mentioned causes. Strictly speaking, diseases are natural processes so combined as to produce a course of action in the body which is not natural.

We have purposely considered first the simplest case of causation of disease, namely that in which changes are set up by some external injury or disturbance; but it is, of course, evident that there are diseases in which no such cause can be immediately traced, or which appear to be spontaneous.

We see (as in our illustration of a revolving body) that, independently of any obvious injurious cause, the body begins to act wrongly.

The heart's action may be weak, nutrition may fail, some part of the body may show signs of overgrowth or decay. Just as in our former illustration, these irregularities may be due to some original defect in the construction of the body. Such defects may be so great as to make the individual not viable; or enough to produce obvious abnormality of function, as in malformation of the heart; or else may be so slight as not to be at first perceived, and yet sufficient to render the body, after a longer or shorter time, unable to perform its ordinary offices. The disturbance first produced may not be serious; but irregularity of function thus set up may lead to other disturbances, and the state of things becomes progressively worse.

In many cases the disturbance will at first appear as if it were merely a disturbance of function, but really it arises because the organs are inadequate for their work.

Let a child, for instance, be born with a pulmonary artery slightly too narrow. No great inconvenience is felt in early life, but as he grows up he shows signs of imperfect access of blood to the lungs, the circulation is obstructed, and at length serious disease is produced.

It is also probable that some people have their tissues less perfectly formed than others, so that they are either more liable to be injured by ordinary causes (of which Hæmophilia, or the hemorrhagic diathesis, is an instance), or else peculiarly liable to be injured by certain special causes.

It is evident that every degree of imperfect function may be met with, and that the effects will be seen earlier or later in life as the defect is more or less serious. Congenital defects of structure, then, give rise to a *second* class of diseases.

In a *third* class of cases the organs and tissues may be competent for ordinary functions, but not for any extraordinary work, so that they soon show the effects of wear and tear. The disturbances thus set up may at first simulate mere errors of function; or they may be unperceived until some sudden failure reveals the change which has been long going on. The circulatory apparatus in people after middle life, or sometimes earlier, always gives, when examined *post mortem*, evidence of wear or strain, which may be seen both in the heart and the arteries.

The change called atheroma, or degeneration of arteries, is as plainly due to excessive internal pressure as corns and callosities on the feet are due to external pressure. These conditions have an inevitable tendency to become worse. The artery, thickened by pressure, obstructs the circulation, and, in consequence of this obstruction, the pressure is still further heightened and the condition of the artery still further deteriorated. The effect of wear and tear upon the nervous system is not less serious, though less apparent, if this be stimulated too often, with insufficient intervals of rest.

It is evident that imperfection of structure will render the organ more liable to these changes, but that even in soundly made organs continuous overstrain will sooner or later produce its effect. The *third* class of diseases then includes those produced by wear and strain.

Even with this we have not quite exhausted the causes of disturbed action. As in our revolving top the initial impulse becomes at length exhausted, so in the human body there are changes independent of demonstrable causes of disease which we can only call senile or due to old age. Whether old age is itself a cause of death may be disputed. Old people generally die of some disease; but what is perfectly clear is, that they have a diminished power of resistance, and succumb to slighter injuries than those whose tissues have not undergone senile changes. Senile degeneration, then, may be said to be a *fourth* cause of disease.

Besides the four causes now distinguished there is also one special quality of organized beings which is sometimes regarded as a cause of disease, viz., heredity or inheritance. But this cause really falls under those already enumerated.

The effect of inheritance, that is, of some transmitted property in producing disease, comes under two heads. In the first place disease may be directly transmitted by either parent to the ovum, so that the infant has the disease when it is born, as in congenital syphilis. There is no essential difference between this and the transmission of the disease—for instance, from a nurse to a child—after birth.

Secondly, there may be transmitted what is loosely called a tendency to disease. By this is meant that the individual will be more likely than others to suffer from a certain disease in after-life. It is clear that what is in this case transmitted is a certain property of the tissues of the body which makes them peculiarly unable to resist the attack of a certain kind of injury; for instance, of cold, improper food, or some particular kind of specific poison. This is the case with hereditary tendency to bronchitis, to eczema, or to tubercular disease.

It is well to remember that a similar inherited peculiarity in the structure or properties of the tissues may confer immunity against specific poisons.

Again, there may be merely such an imperfection of structure that the organs hardly suffice for the performance of ordinary functions, which are accordingly always or often performed not quite adequately. We often see persons who inherit a digestive, a respiratory, circulatory, or nervous system, which, though not actually defective, has a working power below the average. Hence arise, in the course of daily life, slight functional disturbances, not serious in themselves, but by the accumulation of which is at length produced a disturbance grave enough to be called a disease. This is probably the most frequent mode of the so-called inheritance of disease.

Summary.—We may now arrive at a definition of disease as merely an alteration in the normal functions of the body due to some disturbance. The causes of such a disturbance may be classified as follows:

I. *External cause*, or *injury* in the wider sense, including (1) Mechanical injuries or wounds; (2) Physical, from cold, heat, electricity; (3) Chemical, from corrosive, irritant, or generally poisonous substances; (4) Specific, including *animal poisons*, the nature of some of which, as, for instance, the poison of snakes, is not yet clearly known. This class includes also those known to consist of, or to be generated by, *living parasitic organisms*: animal, or vegetable, of which the most important are the bacteria of specific diseases.

Excessive, improper or inadequate supply of food comes also under the head of injury.

The others are internal, viz.:

II. *Congenital imperfection of structure*, whether of organs or tissues.

III. *Effects of wear or strain* if disproportionate to the resisting power of the organs.

IV. *Senile decay.*

With regard to the above classification, it may be remarked that under Class I. are included two divisions of unequal value; that is to say, specific diseases, which form in some respects a class by themselves, and the effects of simpler injuries. But as the lesions actually produced in all these cases are essentially the same, they are placed together.

In Classes II. and III. the effects are cumulative; and the influence of IV. is especially important, as predisposing the body to be affected by injuries.

Finally, it should be observed that causes belonging to all these classes may, and do, act concurrently.

It would be very satisfactory if we could classify all diseases, and the whole subject of pathology, under the head of Causes. But so simple an arrangement of the subject is not possible We cannot say with certainty what are the causes of some diseases; nor, in regard to others, which is the most influential or determinant of several causes which coöperate in producing them. And our notions of what is called the etiology (or study of the causes) of disease have lately been modified in quite unsuspected ways. For instance, with regard to rheumatism, while it is evident that cold has something to do with its production; there are, on the other hand, reasons for thinking it probable that a specific poison—*i. e.*, a microörganism, may be the true cause.

In other cases, such as tuberculosis, the specific poison is quite demonstrable; but some persons appear to be extremely liable, others much less or hardly at all liable, to suffer from it, in virtue of their original constitution.

On these grounds etiology alone cannot be made the basis of pathology. Moreover, it is to be remembered that the processes and changes set up by different causes of disease do not differ so much as the causes themselves. In fact, certain processes are really common to many diseases, and are thus set up by many different causes. Pathology has to study processes themselves, independent of their cause. Inflammation, for instance, is produced by many different causes, but the process set up by these causes is essentially the same in all cases.

Furthermore, while diseases produce various alterations in the original elements of the body, these alterations can only fall under a certain limited number of types, whatever be the cause producing them. Now it is the task of pathology to study the tissue-changes themselves primarily, and the investigation of their causes is a secdary matter. Degeneration or atrophy, or overgrowth, may be the final term of several distinct processes, but yet the condition resulting is the same in each.

The complete study of the causes of disease, again, would involve an exhaustive examination of all the cosmic conditions under which living beings exist, which is obviously impossible. We shall, therefore, confine ourselves to discussing one class of causes—that, namely, of injuries in the widest sense, from the simplest to those highly complex ones which give rise to specific diseases, and describing their immediate effects. To pursue the subject of causes further would be beyond the scope of this work.

The subject of general pathology will, then, naturally embrace two main divisions:

Part I. The Processes of Disease.

Part II. The Causes of Disease.

It might be a question whether, in treating of the processes of disease, we should begin with considering the organism as a whole, or with the consideration of its elementary parts.

If we were treating of the pathology of animals which have no circulation of the blood, we should start with the changes in cells as the basis of all pathological processes. But in the higher animals the composition and distribution of the blood influence all morbid changes in such a marked degree that it is more convenient to take account first of these factors of disease. The treatment of general pathology then begins with a consideration of *alterations in the blood and circulation.* Next it deals with tissue-changes or *disturbances of nutrition,* and lastly with *anomalies of growth.*

One division in a complete treatise on general pathology ought to deal with anomalies of development and monsters; but as this subject could not be properly treated without much detail, it seems best, for the purposes of an elementary manual, to omit it altogether.

CHAPTER II.

VARIATIONS IN THE QUANTITY OF THE BLOOD: PLETHORA AND ANÆMIA.

EXCESS in the quantity of blood in the body is called *Plethora*, deficiency in quantity is called *Anæmia*, if this word is used strictly, but more generally it is employed in a somewhat different sense, which will be explained hereafter.

Plethora or **General Hyperæmia** was formerly thought to be of great importance, and had remarkable consequences ascribed to it. There is still a belief that plethora may be recognized by certain definite characters, especially redness of the face, a peculiar state of the pulse, and other symptoms thought to indicate distention of the vascular system; and that it especially predisposes to inflammatory diseases and to hemorrhage. Practical experience, however, when its results are carefully sifted, tends every day less and less to admit the reality of the condition, or of the dangerous consequences ascribed to it.

It should be remembered that the amount of the blood in the human body generally is very imperfectly known, and can never be determined during life; that this amount must be constantly fluctuating under the influence of its gains, viz., from food and drink; and its losses, by excretion, exudation, and so forth; and that there is no possibility, therefore, of fixing any standard for the normal proportion of blood to the body-weight. Hence we have no means of determining that the blood at any moment is in excess. The only supposed evidence of excess is tension or pressure in the larger vessels, and fulness of the smaller superficial vessels and capillaries. The question of blood-pressure is discussed later on. In the meantime, it is enough to say that the results of observation and experiment in men and animals, show that the addition or subtraction of even large quantities of blood exercises only a momentary influence on the tension of blood in the arteries. The ligature of a large vessel, or the amputation of a limb without loss of blood (as by Esmarch's bandage), causes a rise in blood-pressure of only a short duration, and produces no permanent consequences, though the proportion of blood in the remainder of the body must be greatly increased. Again, numerous experiments on animals (more especially by the physiologists of the Leipzig school) have shown that a large quantity of blood, amounting to one-half or three-fourths of the original blood-mass, may be added by transfusion without any bad consequences in healthy dogs. The excess of blood first accumulates in the veins and capillaries, especially in the abdominal veins, without producing any bad results. The excess of plasma is slowly removed; a considerable part in a few hours, the rest in two or three days, while the excess of blood corpuscles, though it may remain for some weeks, is not permanent. The arterial blood-pressure is raised only for a few minutes after the operation. When very large quantities, amounting to one and a half times or thrice the original blood-mass, are injected, death occurs, and is preceded by an accumulation of blood in the veins and capillaries, especially those of the abdominal viscera. Even in these cases the blood-pressure is not permanently raised above a normal standard. The explanation of these results is that the vascular system is susceptible of very great variation in capacity, and thus adapted to contain a larger, or smaller quantity of blood without any permanent alteration of tension, that is, without any physical consequences of excessive distention or the reverse. There can be no doubt that, as will be afterward explained, a machinery exists which possesses this compensatory or regulative power, and prevents overfilling of the arterial system. Excess of blood can only accumulate, if it accumulate at all, in the veins.

A practical corollary from these results would be, that the extreme dread of over-filling the vascular system, as in the operation of transfusion of blood (in which it is thought necessary to withdraw a corresponding amount of blood to that injected) is exaggerated, and not founded on any basis of positive knowledge. As regards the fulness of superficial vessels it should be remembered that the blood-supply to the head, and even to the skin, is under the control of every special nervous mechanism, and that their fulness is not necessarily an index to the state of the vascular system generally.

The general conclusions, therefore, are: (1) That the existence of true plethora, as a permanent condition, is unproved, and even improbable.

(2) That transitory plethora will overfill the veins, but not the arteries, and, therefore, will not produce the results traditionally ascribed to plethora.

(3) That the symptoms regarded as those of plethora, so far as they actually exist, are rather those of excess of *pressure* in the arteries (which will be considered hereafter), or of special determination of blood to the superficial vessels. The one anatomical fact alleged as a proof of the existence of true plethora is the existence of hypertrophy of the heart without any other obvious explanation. But this is rather a proof of increased arterial resistance than of increase in the mass of the blood.

The only clinical symptoms which agree with those of experimental plethora are those of overfulness of the abdominal veins, such as causes the production of hemorrhoids. These may possibly be made worse, or even originated, by an increase in the whole mass of blood; but even this conclusion is dubious, since there are many other circumstances which may cause an accumulation of blood in these parts.

It has been supposed that a condition equivalent to plethora in its effects may exist, through an excess of red corpuscles in the blood; but though the number of these corpuscles vary very much, there is no proportion of them which we can recognize as excess.

Hydræmic Plethora is the name which has been given to the condition in which the total amount of water in the circulatory system is increased, without any absolute increase in the other constituents. This, of course, involves a qualitative change in the blood, which is more watery than normal. This condition has been produced experimentally by injecting saline solutions or water into the veins of dogs, with results to be noticed subsequently. It is also possibly the condition of blood which is sometimes brought about by disease of the kidneys, with diminished excretion of water. But as it is impossible to discuss this subject without entering on the question of qualitative variations in the blood, we defer its consideration for the present, only remarking that it is difficult to prove the existence of such a condition in the human body.

Anæmia or **Oligæmia.**—Understood strictly, this should mean an actual diminution in the mass of blood. Such a diminution undoubtedly occurs when large quantities of blood are withdrawn, as in the case of excessive hemorrhage. The consequences are increased rapidity and weakened force in the contractions of the heart, with lowering of the arterial pressure. The latter condition is only temporary, the pressure being soon restored to the normal. In cats and dogs, from which even one-fourth of the mass of blood has been withdrawn, the lowering of pressure lasts only a few minutes; probably because the anæmic condition stimulates the vasomotor centre in the medulla oblongata, and thus is caused a contraction of the muscular walls of the arteries all over the body. The vessels thus contract till their capacity corresponds to the diminished volume of the blood, just as in the case of blood being added, the arterial system enlarges in a corresponding degree. We have, therefore, no direct evidence as to actual variations in the mass of the blood, and it is impossible to prove that in any case, recognized as anæmia, there is a real diminution. But there is strong reason to believe that a real diminution does exist in cases of starvation, or virtual starvation from wasting diseases, and in fatal idiopathic (so-called "pernicious") anæmia, as well as, probably, in other forms of anæmia. The evidence of this after death is sufficiently clear, though not reducible to actual weight or measurement. No one accustomed to post-mortem examinations can possibly doubt that in cases of fatal anæmia the actual quantity of blood is very small, and there is not merely a want of coloring matter. On this point I can speak confidently from personal experience.

When a large quantity of blood has been taken from an animal, a restoration of the blood-mass to its original condition gradually takes place. Water is the first blood-constituent to be restored, the reduced volume of blood appearing to cause an absorption from the lymphatics and tissues. This is thought to occur in a few days, or even (experimentally) in a few hours. It is shown by the fact that the blood is *diluted*—that is, more watery than before—and it is possible, though not susceptible of proof, that the original volume of blood may thus be soon reinstated. Next the albumen of the serum is restored, and may be, it is thought, in healthy animals, in a few days; the leucocytes next begin to present their normal proportions; and lastly, but more slowly, the colored corpuscles; so that in a few weeks the condition of the animal is as it was before. There is every reason to believe, though the fact has not been so precisely determined, that the same process occurs after the loss of blood in the human subject.

It is clear that the blood, till the process of restoration is complete, will be different in quality from what it is in health; one or more of its constituents being deficient relatively to the amount of water. During the whole of this process the condition of the blood is what is called clinically anæmia. Hence we see how this name comes to be used for a qualitative, not quantitative, alteration. In fact, by this name are understood several abnormal conditions of the blood, caused by one or more of its solid constituents being relatively deficient.

The name **Spanæmia**, meaning thinness or poorness of blood, is more accurate than anæmia, though not often used.

These conditions, dependent upon an alteration in the *quality* of the blood, will be discussed afterward.

We must now speak of variations in the amount of blood distributed to different parts of the body, or *local hyperæmia* and *local anæmia.*

CHAPTER III.

LOCAL DISTURBANCES OF CIRCULATION.

When the amount of blood in any organ or part of the body is increased, the condition is called Local Hyperæmia; when the amount is diminished it is called Local Anæmia.

Local Hyperæmia.—Local Hyperæmia may be caused by (1) an excessive supply of blood to the part by the arteries; this is Arterial Hyperæmia or Active Congestion; (2) by imperfect removal of blood by the veins; this is Venous Hyperæmia, or Passive Congestion. The capillaries may be overfilled from either of these causes. It is possible there is a Capillary Hyperæmia, caused by obstruction in these vessels; but if there is, it will be with difficulty distinguished from venous.

Arterial Hyperæmia.—In this condition the part is overfilled with arterial blood. The color of external parts is bright red, the arteries being fully injected, and the capillaries overfull of arterial blood.

In extreme forms of arterial hyperæmia produced experimentally in animals, the blood may run through the capillaries without losing its bright red arterial color. But in ordinary pathological conditions the venous circulation is only altered in that it is more rapid. There may be visible pulsation or throbbing. The temperature of external parts is raised, though not above that of the internal organs. There may be swelling or enlargement of the part from distention of the vessels. There is increased excitability of the nerves of the part, and sometimes sensations of warmth, fulness, or itching, rarely actual pain.

This condition is well seen in physiological hyperæmia of the skin, or blushing, in morbid flushing, such as that of the face produced through reflex nervous action by conditions of the internal organs, and in the various forms of *erythema* of the skin. It is distinguished from the redness produced by hemorrhage by the fact that the red color disappears on pressure; and from the redness of inflammation sometimes by the same test; and also by the absence of any signs of increased exudation from the vessels. The same condition has been seen to accompany the functional activity of internal organs, such as that of the stomach during digestion, or of the glands during secretion.

Causes of Arterial Hyperæmia.—The most frequent cause of arterial hyperæmia is a dilatation of the arteries by relaxation of their muscular walls, howsoever produced. This may be termed ***vaso-motor hyperæmia.***

But, in addition, there may be increased pressure in one set of arteries in consequence of the obstruction of other branches dependent upon the same arterial trunk, or upon the shutting off of the blood from some large division of the arterial system. This may be termed *collateral hyperæmia.*

It is thought that hyperæmia may be produced by increased nutritive or functional activity in the tissue-elements, which thus *attract* an increased supply of blood to the part. This may be called attractive hyperæmia. The afflux of blood to the fertilized ovum in the uterus is an instance. But it may be doubted whether the tissues do not act in these cases indirectly, by affecting the nervous and muscular arrangements of the vessels.

Relaxation of the arterial walls, or, in other words, abolition of the vascular tone, may be caused *directly* by the influence of heat, electricity, or chemical so-called irritants, the action of each of which agents produces superficial transitory redness of external parts. But this easily passes into the more permanent redness which indicates inflammation. Similar loss of tone occurs *secondarily* from paralysis of the muscular fibres subsequent to spasmodic contraction, such as is produced by cold or by a blow on the skin. Here we see a transitory anæmia followed by hyperæmia, which lasts somewhat longer, but passes away without permanent results. In certain pathological conditions the consecutive hyperæmia may be so intense as to lead to swelling and the production of a "wheal." This is the "factitious urticaria," produced in some persons by pressing or rubbing the skin with a blunt point. It has no necessary connection with the disease urticaria, and may occur in healthy persons. Certain conditions of the central nervous system also influence the intensity of this hyperæmia and the rapidity with which it is produced, as seen in the so-called *tache cérébrale*, produced by pressure on the skin in some diseases of the nerve-centres, when the tone of the arteries is doubtless interfered with.

But the most common cause of the loss of tone which causes hyperæmia is a vaso-motor disturbance. This may be either:

(1) A paralysis of the inhibitory or vaso-constrictor fibres, especially such as the cervical sympathetic, the splanchnic, etc., and some mixed nerves, as the sciatic.

(2) Stimulation of the actively dilating or vaso-dilator nerves, such as the chorda tympani, the nervi erigentes of the penis, and, under certain circumstances, the nerves supplying muscles.

The former may be called *neuroparalytic* hyperæmia, the latter *neurotonic.*

Neuroparalytic Hyperæmia.—This condition is most clearly seen in the experimental section of the cervical sympathetic in animals, which produces in the whole of the affected side of the head, including the ear, dilatation of the arteries; with intense hyperæmia, rise of temperature, and visible pulsation, contraction of the pupil, and other symptoms not belonging to the present subject, but serving to make the diagnosis of this lesion in doubtful cases. It is important to remember that after a time this condition is reversed, the affected area becoming anæmic.

The same group of symptoms has been observed in man in a few cases of lesion of the same nerve; especially after gunshot wounds. More generally cases in the human subject do not come under observation till a later period, when the vascular symptoms are reversed, or else in a state of transition, some symptoms belonging to the earlier, some to the later stage; though the condition of the pupil, etc., show that the sympathetic is really affected. Disturbance of the vascular system generally by exercise or emotion may reverse the conditions.

The exciting cause in such cases is lesion of the sympathetic by pressure of a tumor, destruction by an abscess, etc.

A case of this kind was observed by the author in a child, in whom the cervical sympathetic appeared to have been injured by the forceps applied during birth. It corresponded to the later period in experimental section of the nerve (*St. Thomas's Hospital Reports*, vol. iii., N. S., 1872).

A similar condition has been seen in wounds of the brachial plexus by a fractured clavicle.

Hyperæmia of the viscera from section of the splanchnic nerve is one of the best ascertained results of experimental pathology; and it is probable that this condition, in a partial form, may occur in abdominal diseases, but no exact evidence has been produced of such a lesion in man.

In animals, experimental section of cerebro-spinal nerves has been found to produce similar hyperæmia, as, for instance, of the brachial plexus—affecting the anterior extremity, and of the sciatic—affecting the posterior.

This condition has not yet found a parallel in human pathology.

Section of the fifth cranial nerve, or some of its branches, in animals, has similar consequences.

In man, lesion of this nerve, or a branch, has often been seen to cause hyperæmia of the iris, the conjunctiva, the cheek, the gums, etc., the origin of the symptoms from the fifth nerve being proved by the loss of sensation in the parts and in some cases by atrophy. The author has observed a case of lesion of this nerve, unmistakably shown by the last-mentioned symptoms, as well as by certain ocular phenomena, in which there was unilateral flushing, precisely comparable to that of sympathetic paralysis.

Neurotonic Hyperæmia.—Dilatation of the muscular walls of the arteries may also be produced by direct irritation of certain nerves—vaso-dilators. This fact is well ascertained experimentally, but there are not many clear instances of the operation of this law in the human body.

One of the best marked cases is that of hyperæmia of the fingers produced by wounds of the brachial plexus, described as "glossy fingers" by Sir J. Paget, and observed in many cases of gunshot wounds by the American surgeons. The lesion must be incomplete—that is, an irritative lesion, not involving complete severance of the nerve (since the latter, in man, does not cause hyperæmia), and does not appear till some days after the wound.

There is elevation of temperature, compared with the healthy side, of one or more degrees; neuralgic pain; and often evidence of inflammation of the nerve. Similar hyperæmia affecting the skin, or the eye, is observed to accompany neuralgia of the fifth nerve, both this and the pain being apparently dependent upon one common irritative cause.

Local hyperæmia of the extremities, especially the foot, accompanied by hyperæsthesia, has been observed by Weir Mitchell, and called erythromelalgia. It is caused by some affection of the nerve-trunks.

Some forms of erythema appear to be due to the same cause.

All these forms of hyperæmia may recur periodically.

Reflex Hyperæmia.—The hyperæmic conditions above described may be caused by a nervous irritation transmitted to the medulla oblongata, and reflected upon the vasomotor nerves. Experimentally, this is shown by irritating the central portion of the trunk of a divided nerve. Pathologically, we have instances in the flushing of the face, either transient or persistent, produced by derangements of the stomach and generative organs. These are generally regarded as of neuroparalytic origin, but may possibly be the result of a direct stimulation transmitted from the nerve-centre—*i. e.*, neurotonic.

Reflex hyperæmia of the kidneys may be produced by irritation of the urethra.

Hyperæmia of the face is often produced by a reflex irritation starting from carious teeth. Some forms of erythema are probably thus produced.

This is probably the explanation of the sympathetic congestions and inflammations; *i. e.*, when from disease, or injury of one part or organ, the corresponding part or the other side of the body becomes affected. This has long been known to occur in the eye, constituting sympathetic ophthamia.[1] The same phenomenon often occurs in skin diseases; for instance, eczema of one hand, produced by some local irritation, may give rise to similar inflammation of the other hand.

In the observed cases of lesion of the cervical sympathetic in man, the corresponding nerve of the other side has always been in some way disordered in function.

Hyperæmia of central origin.—The same nervous disturbances above described, both neuroparalytic and neurotonic, may originate in a state of the central nervous system independent of irritation. This is seen in the familiar case of blushing from emotion, whether of shame or anger. In various morbid conditions of the brain and spinal cord, hyperæmia of certain parts of the skin, in the form of erythema, is seen; *e. g.*, in tabes dorsalis, myelitis, pressure from carious vertebræ, etc.

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[1] Lately, an entirely different explanation has been given of sympathetic inflammation of one eye consequent on disease of the other. It has been said to be due to migration of bacteria along the sheath of the optic nerve from the originally affected eye to the sound one. On such a point, any one but a specialist may well hesitate before giving an opinion.

Consequences of Arterial Hyperæmia.—This condition, if uncomplicated, does not necessarily produce any notable results. But the tissues are in a more vulnerable condition than usual, and a slight injury will set up inflammation.

In certain cases, long-continued hyperæmia produces hypertrophy of the tissues supplied. It is not quite clear why it should not always do so.

CHAPTER IV.

LOCAL DISTURBANCES OF CIRCULATION.—(*Continued.*)

Venous Hyperæmia (*Passive Congestion*).—When blood is imperfectly removed from a part by the veins, these vessels will become distended and show a condition of over-pressure. This over-pressure is transmitted backward to the capillaries, which will become overfilled with blood; and this blood, passing through them slowly and with difficulty, will become venous in character, through loss of oxygen and accumulation of carbonic acid. In other words, the area of the venous capillaries becomes enlarged in proportion to that of the arterial capillaries. It does not appear that the pressure in the arteries is ever sensibly increased, even by a considerable obstruction in the veins, but the current of blood through them must inevitably be retarded.

A part thus affected will show visible injection of the smaller veins and a general bluish or purple tint, due to the capillaries being overfull of venous blood. An external part in this condition will be colder than normal, and show no unusual nervous sensibility or throbbing.

There will often be swelling, which may be due to actual transudation of serum from the vessels, and not merely to fulness.

Causes of Venous Congestion.—The forces which normally maintain the flow of blood through the veins are the force of the heart, acting through the arteries, the sucking action of the thorax on the great veins during inspiration, and the pressure of muscles, made continuous by the action of the venous valves.

Simple weakening of the heart's action does not necessarily cause venous congestion, but defects in the valves causing obstruction to the passage of blood through the heart, produce *general* venous congestion, especially of the extremities. A high degree of this congestion constitutes cyanosis, and leads to changes in the internal organs. Impediments to respiration produce the same result in a less marked degree.

This general congestion is seen notably in the veins of the lower leg and foot, being there aided by the action of gravity, and producing varicose veins with all their consequences. When the circulation is much enfeebled, as in severe fevers, stagnation of blood may occur in the lowest parts of the body—*i. e.*, (in decumbent patients) in the nates, sacrum, shoulder-blades, and posterior parts of the lungs, constituting *hypostatic congestion.* Direct pressure has a share in producing this condition.

Local venous congestion is produced by causes acting on the veins themselves, such as external pressure—*e. g.*, from tumors, the gravid uterus, overloaded intestines, *etc.*; also by dilatation of the veins resulting from previous congestion. In rare cases changes in the walls of the veins, especially inflammation, may lead to coagulation of the blood and consequent obstruction. But more generally these changes are subsequent to the coagulation (*see* Thrombosis).

Consequences of Venous Congestion.—This form of hyperæmia produces more important and permanent consequences than arterial. When a vein is suddenly obstructed, as by ligature, swelling generally occurs, due to a copious transudation of serum, not adequately removed by the lymphatics—in fact, dropsy; but this is not constant, and depends partly upon the amount of blood conveyed by the arteries, so that it is, at all events, much increased, if not caused, by section of the vasomotor nerves, causing arterial dilatation. The pressure in the veins rises till it may equal that in the arteries.

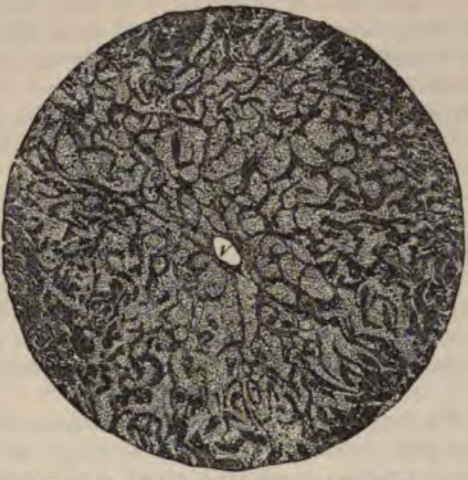
The minute changes which occur may be studied in transparent parts under the microscope. The movement of blood in the capillaries is seen to be retarded, and may oscillate or become stationary unless some collateral channels are opened. The colored corpuscles come in close contact with the walls of the smaller veins and capillaries, which they appear completely to fill, and after a time begin to pass through the walls without rupture, by *diapedesis*. The leucocytes do not pass through unless some further change occurs. The exuded fluid is not identical with normal blood-plasma; it is poorer in albumen, and does not contain the materials of fibrin, so that it does not coagulate. The lymph running from the part has, in experiments, been found tinged with blood-pigment.

The explanation of these facts is, that the walls of the vessels are altered through being imperfectly nourished by the stagnant venous blood, and thus become more permeable to all the blood-constituents. The fact of increased permeability of the vascular wall due to diminished vitality is found in other circumstances also. These conditions are seen to be produced to a great extent in pathological states of venous hyperæmia. The parts become swollen and pigmented from changes in the extravasated blood-corpuscles. If the condition become chronic, there is induration from hardening of the connective tissue, which also becomes hypertrophied. The condition then becomes one of fibroid change or fibroid degeneration.

These changes are well seen in the lower part of the leg when congested from varicose veins. Inflammation does not necessarily follow, but the parts are in such a state that inflammation is readily excited; and hence we find inflammation of the skin, or eczema, frequently resulting from this condition. As the tissues are badly nourished from the deficient supply of arterial blood, atrophy is a constant result, and sometimes we find necrosis set up by slight causes, so that in the skin of the leg ulcers are formed. In parts which are susceptible of great vascular dilatation, such as the bed of the nail and ends of the fingers, permanent enlargement occurs, forming the condition known as "clubbed fingers."

The changes in internal organs are not less clearly marked when examined after death. In venous congestion from obstruction at the heart, the liver and kidneys are most strikingly affected. The liver is at first enlarged, and if examined in that stage will be found very full of blood, with the central portion of the lobules especially engorged (Fig. 1). At a later stage the organ is found smaller. The central portion of each lobule shows dilatation of the capillaries, but wasting of the liver-cells, which are deficient there, and also deposition of pigment. In the outer portion the cells are engorged with fat. The contrast of color between the two portions produces the appearance known as nutmeg-liver. The organ is also hard from induration, and, probably, increase of the connective tissue. The functional activity of the organ is diminished.

FIG 1.



Lobule of liver in chronic venous congestion.

V=vena centralis. Around this the liver-tissue is rarefied, and replaced by distended capillaries containing blood. Numerous pigment-granules. The outer margin of section shows more liver-tissue.

The kidneys are also at first enlarged, and of a slaty-blue color. After a time atrophy sets in, and the fibrous tissue relatively predominates, so that the condition resembles, though it is not identical with, primary fibroid change. The functional activity of the kidney as a secreting organ is lowered, but there is often observed a passage of blood-serum into the urine, or *albuminuria.*

When the portal circulation is obstructed, as by cirrhosis of the liver, similar changes are found in the organs connected with the portal system. The spleen is enlarged and much congested. The mucous surfaces are congested and readily pass into catarrhal inflammation, diarrhœa, or gastric catarrh. Hemorrhages from rupture of small vessels often occur. The serous surface of the peritoneum becomes œdematous, and readily gives off a serous effusion, constituting

Increased pressure on the hæmorrhoidal veins will te
dilatation of these vessels, and hæmorrhoids, though this i
the causes of the production of these tumors.

The spleen, being an organ capable of great vascular dilatation, becomes permanently enlarged.

In obstruction of the right side of the heart (direct or secondary) the lungs become first congested, and then pass into a condition of brown induration, characterized by hardness and pigmentation, from the escape of blood-corpuscles.

Collateral circulation through neighboring veins is often established in cases of venous obstruction, and by this means the consequences are often averted or minimized. The resulting dilatation of superficial veins is often the only external evidence of the obstruction of internal veins.

In the cases we have been considering there must be some collateral circulation. If there be none, so that there is an absolute stoppage of circulation, the result is local death, or necrosis—a condition to be considered hereafter.

Capillary Hyperæmia—Stasis.—It has been shown that fulness of the capillaries is a consequence both of venous and of arterial hyperæmia. Whether it may also be caused by a change in the capillaries themselves is rather a difficult question. Though capillaries are capable of contraction, the change of calibre thus produced is not enough to cause serious obstruction. Hindrance to the passage of blood through the capillaries, if caused at all, must be by a change in the capillary wall, altering the relations between the blood and the vessels, and producing greater friction—that is, greater resistance.

That such a change is possible is shown by the results of experiments on animals.

If the web of a frog's foot be touched with some moderately stimulating substance, such as mustard or alcohol, while the circulation is being observed under the microscope, there is observed (besides the dilatation of the smaller arteries spoken of above) a peculiar change in the capillaries. They become dilated. The blood-current becomes slower in them, and the distribution of the blood-corpuscles loses its *axial* character. The red corpuscles come closer to the walls, and are, therefore, diffused through the whole width of the channel, being mingled in one mass, with the white corpuscles.

The circulation becomes slower and slower, till at length the vessels appear distended by a mass of corpuscles, with little intervening fluid. Finally, the circulation may stop altogether, and the corpuscles become so closely pressed together that they appear to lose their outlines, and look as if fused together in one homogeneous mass.

The condition is most marked in the capillaries, but the neighboring small veins are also affected in some degree in the same way, a capillary area forming a sort of centre, round which the change is diffused into the neighboring venous and arterial channels.

If the irritation be not too prolonged, the stagnation gives place to motion, and the normal circulation is reëstablished. If stagnation be too prolonged, the only result can be local death, or necrosis. This condition is called *stasis*. It has been regarded as a necessary part of the process of inflammation. Nevertheless, inflammation may occur without stasis, and stasis without inflammation. The main distinction, as will be seen afterward, is that in stasis the passage of blood through the affected area is hindered, and the total amount lessened; whereas in inflammation the whole amount of blood passing through the part is greatly increased. The cause of this change must lie in the capillaries, since the condition of the arteries and veins does not account for it. It must be caused by a change in the relations between the blood and the capillaries. Either the walls of these vessels are changed in such a way as to retard the blood-current by producing greater friction, or the blood in that part is so changed as to pass through the vessels with greater difficulty. There is probably some change in the blood, which may very likely, in the thin tissues of the frog, suffer some loss of fluid by evaporation; but the more probable supposition is that the chief change is in the walls of the capillaries.

There can be no doubt that, normally, the condition of the vascular wall, especially in the capillaries, exercises an important influence in maintaining the "vital equilibrium" between the blood within the vessels and the tissues outside. It is owing to this that the normal interchange of fluids takes place between the vessels and the tissues, and that the normal flow of blood is maintained, in which the corpuscles move along in the middle of the stream without touching the walls, leaving the clear "plasmatic layer" around. When the walls are altered, these relations are disturbed, with what results has been seen. A convincing proof that the cause of stasis is in the vessels themselves, is furnished by the experimental result that when a neutral fluid, as milk, is circulating in the vessels of a frog, instead of blood, stasis may be determined by the action of local irritants, and the milk then stagnates in the same way as blood in the parts affected. It is, however, quite possible that the capillary circulation is influenced by the condition of the tissues outside even more than by the condition of the capillary wall itself. If so there would be an indirect action of the tissues, through the capillary wall, on the passage of blood; and if the tissues were injured, retardation would result. This point, brought out by the researches of Landerer, will be further considered in speaking of inflammation.

The experimental stasis, as above described, is most easily produced in frogs. In warm-blood animals, as in the wing of the bat, it is only partially and with difficulty obtained.

There is some doubt as to what pathological conditions in the human body correspond to the stasis produced by experiment. About internal conditions we know nothing, but the stagnation produced in the skin by cold, and sometimes arising from other obscure causes, as in one form of erythema, may be an instance. Blood which stagnates in the human skin must become venous, and hence the color of parts in the condition of stasis will be the same as in venous congestion.

Hence the condition of cyanosis of the extremities, or "local asphyxia" (of Raynaud), appears to be a condition of stasis, th caused primarily by arterial disturbance.

It is probable also that a stagnation of this kind is the percur ulceration of the legs, in the general retardation produced by venous obstruction or dilatation in the lower extremities.

The relations of stasis to inflammation will be spoken of afterward.

Local Anæmia.—This occurs whenever the blood-supply to an organ or part is cut off by obstruction of the nutrient artery, from whatever cause.

Ischæmia is the name given when the obstruction to blood-supply is partial only.

If an artery or branch be obstructed, there will necessarily be temporary anæmia of the part supplied; but if there be a sufficient collateral anastomosis, the blood-supply will be restored, as we see after ligature even of the main artery of a limb.

Even if there be no true arterial anastomoses there may be an oozing backward of blood from the capillaries into the part the arterial supply of which is cut off. The condition produced is called infarction, and will be described under the head of Embolism. It is not anæmia.

But if there is no restoration of the blood-supply, the part will remain anæmic, and undergoes local death or necrosis. If the part be in contact with the air, or is any other way exposed to septic influences, such as the neighborhood of the intestinal canal with its contents, gangrene or putrefactive necrosis is set up. If the part be secluded from the air it undergoes decay, or pale necrosis without putrefaction. If the tissue be one of which the nutrition is very easily disturbed, such as the brain, there is rapid *softening*, the substance becoming converted into a pulp, in which may be found cells in a state of fatty degeneration, fatty and albuminous granules, blood-pigment, and other products of disintegration.

In other parts a slow process of shrivelling and atrophy may be set up. Something like this we see when one renal artery is totally blocked. The kidney is changed into a hard, fibrous-looking diminutive of the original organ. But in this case, and probably in others of arterial obstruction, there must be some other source whence the anæmic part derives a scanty but constant supply of blood. In the kidney this may be effected through the capsule, which not only has sometimes a small supply from the suprarenal artery, but has capillary anastomoses, which may become enlarged, with the peritoneal vessels, and thus with the portal system. Such connections may sometimes be seen very prominently in cases of obstruction of the portal veins by cirrhosis of the liver.

True complete anæmia of a part is not a very common occurrence. It may be caused by

(1) Arterial thrombosis or embolism, which will be spoken of later.

(2) Arterial obstruction through inflammation of the inner coat. This condition, or endarteritis obliterans, is mostly, if not always, a consequence of syphilis.

(3) Arterial spasm. This has been thought to be the cause of epilepsy, of hysterical amaurosis and of neuralgia, through affection

of the cerebral, retinal, and other arteries respectively; but the proof is not complete.

One form of spasmodic anæmia, known as Raynaud's disease, is well seen in external parts. The usual phenomena are as follows: Portions of the extremities, hands, or feet, sometimes the tips of the ears, become suddenly and perfectly bloodless, and this condition lasts for some minutes, hours, or even days. The change is generally symmetrical on the two sides of the body. The affected part is pale, cold, and pulseless. In slight cases the skin and superficial parts only are affected; in more severe cases the whole thickness of fingers, toes, or limbs.

If this condition should last long enough, gangrene results; but generally the anæmia passes away slowly or suddenly.

As it goes away the parts become blue or cyanotic, though still cold, and thus present the appearance of venous hyperæmia or local asphyxia, mentioned above.

But there is this capital distinction, that in the condition now spoken of there is less than the normal amount of blood, not more, in the part. The cyanotic color then will be due merely to slow passage of blood through the capillaries, so slow that the blood loses oxygen, absorbs carbonic acid and becomes venous in character, not being replaced with sufficient rapidity by arterial blood. The condition, then, even in the cyanotic stage, is one of partial anæmia.

The sudden onset and sudden passing away of this form of anæmia make it pretty certain that it must be due to spasm of the annular muscles of the arteries. The origin of this spasm would, from the symmetrical character of the affection, appear to be in the central nervous system, but what change in that part sets it up is still obscure.

Similar anæmia from spasm has been produced experimentally by direct electric stimulation of the vessels, or by stimulation of the sympathetic nerve-fibres distributed to them.

Another form of local spasmodic anæmia ending in gangrene is seen in ergotism, the disease caused by eating rye affected with the ergot-fungus (*Claviceps purpurea*). This occurs epidemically in countries where rye-bread is used for food, and was at one time not unknown here.

(4) That pressure from without upon an artery may cause obstruction is sufficiently obvious; but it is not a common cause, arteries having much greater power of resistance to pressure than veins.

Ischæmia, or partial anæmia, occurs as a consequence of partial arterial obstruction from thickening or inflammation of arteries, especially in *atheroma* and endarteritis obliterans.

As such a change must be gradual, its symptoms will not be very marked, but it is undoubtedly a cause of atrophy, especially of senile atrophy as affecting various tissues. It will be further noticed under that head.

Obstruction, not quite complete, of the main artery of a limb, may, as we have seen, produce stagnation of the circulation without the appearances generally considered as indicating privation of blood.

There is some reason to think that the affections of the lower leg, chronic eczema and ulcer, usually produced by venous congestion, may also be in some cases due to arterial obstruction. I have seen some cases suggesting this, where there was great obstruction of the external iliac artery by atheroma.

Signs of Hyperæmia and Anæmia after Death.—The characters of general anæmia and hyperæmia have already been spoken of. The recognition after death of local disturbances of circulation, or anomalies in distribution of blood, presents some difficulties, and is best considered with reference to the different classes of vessels.

Arteries are generally empty after death, unless, from a diseased condition of their walls, they are unable to contract. Hence, simple arterial hyperæmia leaves, as a rule, no traces after death. The same is true of slight degrees of inflammation; for instance, in cases of acute bronchitis, where there are unmistakable signs of acute inflammation during life, the mucous membrane will sometimes, after death, be found normal, as regards the amount of blood contained in it.

The larger veins, on the other hand, are always found more or less full after death. The amount of fulness depends chiefly upon the mode of death. In death from asphyxia, which is the commonest form, the right side of the heart and the veins are always engorged with blood. In death from syncope or diastolic arrest of the heart, the blood is more uniformly divided between the two sides of the heart, and some clots may be found in the aorta, though the smaller arteries are empty, unless diseased, while the veins are full, but less strikingly so than in the asphyxial mode of death.

The most important post-mortem evidences of hyperæmia is obtained from the condition of the smaller veins, smaller arteries and capillaries. Visibly injected vessels must be veins or arteries; it is not always easy to say which; but their nature, if not obvious to the naked eye, may be determined by their anatomical distribution, or (as pointed out by Virchow) by tracing their connections.

True capillary vessels, it should be remembered, are not distinguishable by the naked eye, but if overfull, impart a general red color to the part.

Whether this diffuse redness is due to arterial or venous hyperæmia *cannot be determined by the color alone.* All blood in the dead body, if secluded from the air, has a dull red, more or less venous tint. When exposed to the air, if the hæmoglobin be not too much decomposed, it will assume a bright arterial color.

This change may often be seen taking place while the autopsy is in progress; as, for instance, on the exposed surfaces of coils of intestine, or in the pia mater, or in the lungs when the cavities are opened or the organs removed from the body. This change of color is especially noticeable in the lungs of children.

In some cases of disease the blood is said to lose the power of absorbing oxygen after death.

To recapitulate the heads of this most important topic, general fulness of the smaller vessels of a part, with diffuse redness, constitutes congestion or hyperæmia. It can only be determined to be morbid by reference to a standard—*i. e.*, by comparison with the same organ free from disease, and examined under similar circumstances. Whether the congestion is arterial or venous is to be determined not by the color, but by the respective fulness of the smaller veins and smaller arteries. Fulness of the arteries, if certainly established, is always a sign of disease, and, generally speaking, of inflammation of the part.

Certain fallacies which beset the post-mortem determination of hyperæmia may be briefly noted.

Post-mortem staining of the tissues by the coloring matter of the blood produces an appearance often mistaken for inflammation or congestion.

The blood in a normal state, soon after death, does not stain the tissues or even the vessels in which it is contained; but when decomposition sets in, the blood-pigment diffuses into the serum, and stains the walls of the vessels and afterward other parts. In certain diseases, especially severe fevers—typhus, typhoid, diphtheria, etc.—the decomposition of the blood is unusually rapid, and, hence, staining of the bloodvessels and organs is to a certain extent a post-mortem sign of such diseases. It also occurs after death from chloroform or ether or carbonic oxide poisoning, and, probably, in some other kinds of poisoning.

This condition, the so-called "dissolved state of the blood," may occur during life, but is an extremely rare occurrence. It is evidenced, for instance, by the passage of hæmoglobin, without corpuscles, into the urine, or *hæmoglobinuria.*

Staining of the inner surface of the aorta or large arteries from this cause has sometimes been mistaken for inflammation or *arteritis.*

A peculiar form of post-mortem imbibition is often seen in the stomach, when, by the action of the gastric juice on the blood contained in the vessels, the appearance of excessive vascular injection, or a diffuse staining, is produced. Hence, the determination of true congestion or inflammation of the stomach, so important in cases of poisoning, is a matter which requires especial care.

Certain poisons, as arsenic, impart a particularly brilliant color to the blood with which they are in contact, whether the blood be actually present in excess or not.

A very intense red color of any organ after death always raises the suspicion of its being due to minute hemorrhages, which are often seen in the membranes of the brain, and in highly congested kidneys. This point can hardly be cleared up without microscopic examination.

The determination after death of a condition of chronic venous congestion usually presents no difficulty, if, in addition to vascular fulness, we have the characters already pointed out as being the consequences of venous hyperæmia.

Distribution of the Blood in the Body after Death.—It should be remembered that, in making post-mortem examinations, the amount of blood apparently contained in different parts is affected by the order in which the different cavities of the body are opened. If the head is opened before the thorax, it will appear fuller of blood than when it is opened after the great vessels of the thorax have been divided.

The vascular fulness of the abdominal organs, especially the intestines, is best judged of when they are examined without being disturbed, and before the thorax is opened.

Blood in the body after death obeys, to a certain extent, the law of gravitation; and this is especially the case if it long retains its fluidity. Hence, it collects in the lowest parts, as the body lies; and this being usually in the supine position, the back, the spinal cord and its membranes, the posterior part of the brain, the posterior bases of the lungs, etc., will always appear very full of blood.

This condition is called *hypostasis* (*i. e.*, settling down) or, less properly, hypostatic (*i. e.*, sedimentary) congestion, and must be carefully taken into account in determining the congested state of organs.

A true hypostatic congestion may occur before death, in feeble states of the circulation, as in adynamic fevers (*e. g.*, typhoid), or in chronic diseases where patients have been long in bed. It is especially seen in the posterior parts and bases of the lungs, which are much engorged.

The distinction of hypostatic congestion, seen after death, from post-mortem hypostasis, requires care.

CHAPTER V.

ŒDEMA AND DROPSY.

THE word *œdema* means swelling, but is specially used for swelling of connective tissue by the accumulation in it of an excessive quantity of serous (albuminous) fluid.

Dropsy (or *Hydrops*) means an accumulation of such fluid in those parts, as well as in the serous sacs and cavities of the body. In German (and some English) works the word hydrops is used only with reference to these cavities; but usually, in this country, it is employed in the more general sense given above.

Anasarca is used for œdema of the skin and subcutaneous tissue, in which the surface when indented, as by the finger, shows a permanent depression, through having lost its elasticity—*i. e.*, "pits on pressure."

Accumulations of fluid in the different cavities receive different names, as *Ascites* for dropsy of the peritoneum; *Hydrothorax*, of the pleura; *Hydrocele*, of the tunica vaginalis; *Hydrocephalus*, of the ventricles of the brain; *Hydropericardium*, which explains itself.

General dropsy is when the condition affects the whole body, or a large part of it.

The connective-tissue spaces and serous cavities normally contain a certain amount of fluid, which passes into them by transudation from the blood-capillaries, and is removed by the lymphatic vessels and veins. The amount is regulated by a balance between what is thus sent into them and thus removed. Dropsy consists in a disturbance of the balance; the normal amount being increased either by (*a*) increased transudation from the blood, or (*b*) impeded removal of fluid.

a. **Increased Transudation.**—This may depend upon (1) hyperæmia causing increase of blood-pressure; (2) a condition of the blood which makes this transudation easier; (3) a change in the capillary wall which renders it more permeable to the transudation.

(1) *Arterial* hyperæmia, though it increases the capillary blood-pressure, does not of itself cause increased transudation, or, if any, not more than the absorbents can easily carry away. It is, therefore, not a cause of dropsy.

Venous hyperæmia, on the other hand, regularly causes increased transudation, shown by the increased flow of lymph, and, if it reaches a certain point, must produce dropsy. The conditions which give rise to this have been already explained in speaking of venous hyperæmia (p. 24). It is clear, then, that it is not rise of blood-pressure alone, but the changes which follow venous obstruction, that are the cause of dropsy.

In animals, tying the chief vein of a limb does not produce dropsy of the limb, but will do so if there is some concurrent cause; *e. g.*, if the whole limb be enclosed in the ligature so as to stop the lymphatic circulation simultaneously with the venous; or if the chief nerve of the limb be divided.

The most marked form of dropsy is produced when the veins are obstructed, and at the same time arterial hyperæmia is produced by vasomotor paralysis. This condition has been produced experimentally by tying the vena cava of a dog, and at the same time dividing the sciatic nerve of one limb. Ranvier found that under these circumstances œdema occurred only in that limb of which the sciatic nerve was divided; though both limbs were in the condition of venous hyperæmia. But in man it is often seen that obstruction of the chief vein of a limb, by *thrombosis* or coagulation, rapidly produces œdema, without the concurrence of any arterial hyperæmia.

(2) The condition of the blood which predisposes to increased transudation is an excess of water, either absolute as hydræmic plethora, or relative, as hydræmia (see Chapter II.).

The former condition is that which occurs in affections of the kidney, when the excretion of water is diminished, and hence it accumulates in the blood.

There is no doubt that weak albuminous solutions diffuse through dead animal membranes more rapidly than strong solutions, and in proportion to their lesser specific gravity. Hence it has been concluded that the same would be the case with the walls of capillaries, and that a watery condition of the blood must cause rapid transudation.

This explanation of the dropsy caused by kidney diseases has been generally received; but lately doubt has been thrown on it by the experiments of Cohnheim and Lichtheim, who found that production of artificial hydræmia by injection of immense quantities of water or neutral solutions into the vessels of dogs or other animals, did not produce dropsy of the limbs or the skin. The excess of water was excreted by the kidneys, intestines, salivary glands, liver, and pancreas; and, along with increased discharge from these organs, was a marked œdema of all of them, as well as of the abdominal organs generally, including the peritoneum. Corresponding with this condition was an enormous increase of the flow of lymph through the thoracic duct.

On the other hand, there was no increase in the flow of lymph from the lymphatic vessels of the limbs. The lungs were rarely affected, but in some cases became œdematous. It is concluded from these experiments that hydræmic plethora by itself, without some other morbid change, does not produce increased transudation from the vessels. That is, the capillary wall, if healthy, does not behave like a dead membrane, like a simple mechanical filter.

Varying the experiment so as to produce dilution of the blood without increase of its quantity—*i. e.*, simple hydræmia or hypalbuminosis, there was no increased excretion of water from the above-mentioned organs, and equal absence of increased transudation from any part of the vascular system.

If, however, venous hyperæmia of any part is produced in an animal, which has been brought into the condition of hydræmic plethora, as, for instance, by tying the femoral vein, the leg thus affected becomes dropsical.

This result does not follow in the condition of pure hydræmia unless the condition has existed some days; but then dropsy of a limb follows ligature of the vein as in the other case.

The conclusion, then, is, that while a watery state of the blood does not of itself produce dropsy, it acts as a powerful concurrent cause when another condition—namely, venous hyperæmia—comes into play.

(3) *Changes in the Vascular Wall.*—It is maintained by the school of Cohnheim that a change in the capillary wall, making it more permeable to fluids, is the most important factor in the production of dropsies.

Thus, when a hydræmic condition is kept up for some days, it is argued the capillary wall is badly nourished, and passing more into the condition of a dead membrane, permits increased transudation.

Also a very slight degree of inflammation—that is, injury of the minute vessels—produces local dropsy when the condition of the blood is such as to favor it.

The same condition is produced, as will be shown presently, in many of the diseases of which dropsy is a feature; such as general cachexia and anæmia, chronic heart disease, and more especially kidney diseases, in which there is great loss of albumen by the urine. It has often been observed that, in famines, those suffering from starvation are liable to dropsy.

b. **Impeded Removal of Fluid.**—Dropsy from inadequate removal of fluid, or obstructive dropsy, may be caused by obstruction of the lymphatics or of the veins.

Obstruction of the lymphatics is not found to be a powerful cause of dropsy. If the lymphatic vessels of a limb be tied as completely as possible, no œdema is, generally, produced. This negative result is probably due *first* to the fact that it is impossible quite to stop the lymphatic circulation, owing to the number of anastomoses of the lymphatic vessels, and also that new channels are rapidly developed; *secondly*, to the power which the vein possesses of absorbing fluid from the tissues and thus taking up the deficient function of the absorbents.

Even stoppage or ligature of the thoracic duct, causing engorgement of the whole lymphatic system, does not regularly produce dropsy, though it has done so in some instances.

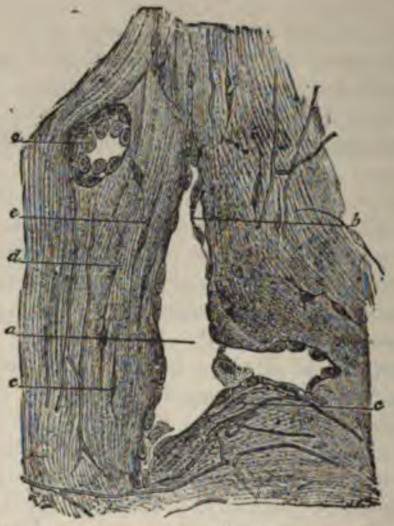
Obstruction of the veins, on the other hand, is the most important of the mechanical causes of dropsy.

Complete stoppage of the venous circulation in a limb constantly leads to œdema in the human subject; but in experiments on animals —*e. g.*, tying the femoral vein of a dog—this result does not generally follow, though it will do so if some of the causes above-mentioned coöperate.

The difference probably depends on the more perfectly healthy condition of the vessels and tissues in the animals operated upon. It is a matter of degree, for, even in man, œdema dependent on venous obstruction may be removed by slight causes, as, for instance, by keeping the affected limb elevated or horizontal instead of pendent.

The reasons why venous obstruction causes increased transudation are sufficiently obvious from the consideration of the conditions of venous hyperæmia already pointed out (p. 24). But in addition we have the important fact that the veins can no longer act as absorbents, and thus the lymphatics are inadequate to carry off the excess of transuded fluid; so that the action of venous obstruction is twofold.

FIG. 2.



Lymphatics in œdema of the skin (CORNIL and RANVIER).
a, cavity of the vessel; *b*, its endothelium; *c*, connective-tissue cells; *d*, fibrous bundles of connective tissue, among which is some elastic tissue.

There is evidence that in dropsy there is a greatly increased outflow of lymph, through the lymphatic vessels. They are found (as in Fig. 2) greatly dilated, so that small, hardly perceptible interfascicular spaces in the connective tissue become dilated into considerable vessels.

It is by this means doubtless that œdema of a limb, or other parts, is kept stationary instead of increasing indefinitely, and by these channels probably that dropsical effusions are chiefly absorbed or removed.

Composition of Dropsical Effusions.—The fluids poured out in dropsy contain albumin, but less of it than does the plasma of the blood (*liquor sanguinis*), and less than the exudations of inflammation. More rarely small quantities of fibrin are present, but the liquid usually coagulates on the addition of a fibrin-ferment.

The following table (chiefly from Hoppe-Seyler) gives the results of some analyses of serous fluids.

	Water.	Albumin.	Fibrin.	Salts.
Normal blood-plasma	903	79	4	8.55
Lymph	939	43	0.	...
Normal cerebro-spinal fluid	987	2.2	...	9
Hydrothorax	957	28	...	0.14
Ascites	960	30	...	8
Anasarca	982	3.6	...	9
Cerebro-spinal fluid in dropsy	983.54	...	...	...
Hydrocele	939	49	0.6	9

In general, serous effusions in the pleura are the richest in albumin, peritoneal effusions less so, and those of anasarca or subcutaneous œdema the most watery. C. Schmidt examined, in a case of renal dropsy, the fluids removed after death from the pleura, the peritoneum, the subarachnoid space, and œdematous connective tissue; finding the proportion of water to be 964, 979, 984, 989 in a thousand respectively.

Clinical Forms of Dropsy.—Dropsy, as met with clinically, is caused chiefly by either (1) obstructed circulation; (2) cachexia; (3) kidney disease. Rarely it appears to be due to (4) nerve-derangements, or neurotic dropsy. Besides these we have to distinguish inflammatory œdema, sometimes called inflammatory dropsy.

(1) Dropsy from obstructed circulation may be *local*, from obstructions in veins, or *general*, from some impediment to the action of the heart. When the heart's action is interfered with either by disease of the valves, especially of the right side, or, what is more common, when the right side is secondarily affected by disease of the left side, or when its action is obstructed by some affection of the lungs, or when its substance is weakened by fatty or other degeneration, the whole venous circulation is retarded and dropsy is liable to occur. Nevertheless it is only produced when the heart-disease is of long standing, and hence degeneration of tissues, leading to changes in the vascular wall, and deterioration of the blood, are powerful concurrent factors. Emphysema of the lungs, and chronic brochitis, by retarding the circulation, act in the same way.

Cardiac dropsy is distinguished by affecting especially the lower limbs and other dependent parts of the body, the serous cavities, and the lungs (œdema). The face is rarely, if ever, affected. However, in a late stage, the dropsy may be very nearly universal.

Local dropsy of the peritoneum, from obstruction of the portal vein, constitutes *ascites*.

(2) Cachectic dropsy is seen in anæmia, chlorosis, malarial cachexia, scurvy, etc. It may also result from long-continued slow starvation, as in famines. It affects chiefly those parts where the action is aided by gravitation, as the lower limbs, but may be very general.

It must be admitted that the explanation of some forms of dropsy is very difficult; though they may be provisionally placed under this head.

(3) *Dropsy from kidney disease, or renal dropsy*, is seen more especially in those forms of Bright's disease where the amount of urine is diminished and there is a great loss of albumen. It comes on very rapidly in acute inflammation of the kidney. But in those cases where little albumen is lost and the amount of urine is not diminished (contracting granular kidney), it is an infrequent, or at least a late symptom.

The chief factor in renal dropsy is probably the deterioration of blood by loss of albumen, which lowers its specific gravity. This favors transudation, either directly or secondarily by causing degeneration of the vascular wall. It is doubtful, as we have seen, whether retention of water in the blood is a direct cause of dropsy, but there can be no doubt this has great effect when the condition of dropsy is once established. It is a definite clinical fact that in kidney disease increased excretion of water, or *diuresis*, diminishes dropsy, while diminished excretion, or *anuria*, increases it.

For instance, in healthy persons the amount of water passed by the kidneys is about three-quarters of that taken in. In a case of kidney disease (parenchymatous nephritis) with dropsy it may be only one-half, or a quarter, or even less; and diminishes as the dropsy increases. But when the dropsy passes away, the excreted water may be equal to, or even slightly more than that taken in. When the dropsy is stationary, not increasing or diminishing, the excreted water may be two-thirds of that ingested. All these variations have been observed in a single case (Bartels).

It follows that, although diminished excretion of water may not be the original cause of renal dropsy, it is a most powerful concurrent factor, and the chief factor in causing its variations.

The clinical type of renal dropsy is very different from cardiac. It affects, first of all, those parts where the connective tissue is lax and easily distended—*e. g.*, the eyelids, the prepuce, the scrotum—and may sometimes be seen in the conjunctiva of the eye when it is present nowhere else. It is of course assisted by the action of gravity, and hence often appears in the lower limbs. Later on it affects the subcutaneous tissue, the serous sacs, the lungs, the brain, etc.; in acute or extreme cases, the connective tissue generally, external and internal.

(4) *Dropsy of nervous origin.*—It has been thought by some that nervous influence has a large share in producing œdema or dropsy. When it does so it is probably by paralyzing the vasomotor nerves, and causing hyperæmia, which, in combination with some other obscure factor, leads to effusion.

In paralysis, œdema of the affected limbs sometimes, though rarely, occurs. It is most often seen in infantile paralysis (or anterior poliomyelitis), where there are marked changes in the nutrition of the parts, in addition to impairment of motion or sensation.

In affections of the trigeminus (fifth) nerve, œdema of a part of the face is sometimes observed.

When any other cause leads to general dropsy, it is probable that a disturbance of innervation determines its incidence on any particular part.

Inflammatory Œdema or **Dropsy** is generally distinguishable from true dropsy. It occurs in distensible connective tissue, which is either the seat of a slight inflammation or in the neighborhood of an inflamed part. For instance, a small abscess at the root of a tooth may cause diffuse œdema of a large part of the face. A similar condition occurs in serous sacs, where the distinction is more difficult.

Hydrocele may be regarded as on the border-line between the two conditions, but on the whole appears to be an inflammation of the tunica vaginalis.

The essential distinction is that the exudation in inflammatory œdema or serous inflammations contains more albumen than in true dropsy, and is more often coagulable, from containing the elements of fibrin.

Cohnheim, however, applies the name of inflammatory œdema to certain forms—*e. g.*, the dropsy following scarlatina—which are generally considered as passive or non-inflammatory.

CHAPTER VI.

HEMORRHAGE.

By this term is meant the passage of blood with all its constituents out of the vessels. Transudation of plasma or serum alone, or of hemoglobin if dissolved, or of leucocytes with fluid constituents, is not enough.

Hemorrhage may be arterial, venous, or capillary, according as one of the three classes of vessels is its seat.

It may occur by soaking or creeping of the elements through the walls, called Diapedesis, or by rupture of the walls, which may be called Rhexis. The former occurs in capillaries and smaller veins only, the latter in all classes of vessels. Hemorrhage from all vessels of a particular area at once constitutes parenchymatous hemorrhage.

Hemorrhage by Diapedesis.—This is, as has been seen, a regular consequence of venous engorgement, if sufficiently intense. It is also seen in stasis, and often in inflammation.

In these cases it may, in transparent parts, be watched under the microscope.

The question how the corpuscles find their way through the unbroken vascular wall is a difficult one. It has been supposed that the capillaries (more especially) possess normally small openings, *stomata*, in their walls, through which the corpuscles pass. This view is, however, now generally abandoned; and it is thought that there can be only at most some separation of the (endothelial) plates constituting the capillary wall along their lines of juncture.

It is not certain, however, that there is any mechanical change in the capillary wall, but there may be only a change in its substance which makes it more permeable. If this be so, the corpuscles pass through the wall, as they might through a film of gelatine, which closes again behind them.

The phenomenon has also been explained as a consequence of mere pressure, but it does not appear that, according to physical laws, fluid pressure could act on a solid body in the fluid so as to force it through in such a way.

Hemorrhage by Rupture.—This will, of course, occur as a consequence of a pressure, however produced, sufficient to burst the vessel. But it will generally be found that the vessel has been weakened by some morbid change before this occurs.

In arterial hemorrhage it is a broad, general rule that no amount of pressure, such as occurs from disturbances of the circulation, will suffice to break the walls of a perfectly healthy artery. It has been found experimentally that the carotid artery of a dog will bear fourteen times the normal blood-pressure without bursting. External violence or wounding may, of course, rupture the wall; or the artery, itself healthy, may be eaten away by gangrene, ulceration, or suppuration.

Hemorrhage from sloughing, secondary hemorrhage after amputations, and that from ulcer of the stomach, are instances. The author has seen fatal hemorrhage from the internal carotid artery consequent on abscess of the tonsil (*St. Thomas's Hospital Reports*, vol. xii. p. 131), but such cases are rare.

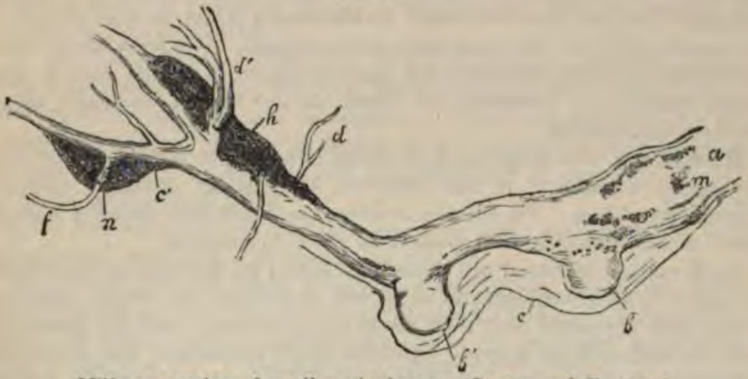
The conditions of the arteries which predispose to rupture are fatty or atheromatous degeneration, including calcification, and the formation of irregular or saccular dilatations, called aneurisms, especially those of small size, called miliary aneurisms. These conditions are most common in the arteries of the brain, but also occur elsewhere.

Increased blood-pressure will also be evidently a predisposing cause.

Severe cerebral hemorrhage is nearly always traceable to the rupture of a small aneurism, either a miliary aneurism (see Fig. 3) or one of larger size.

The cause of the production of miliary aneurisms is not quite clear; but probably high blood-pressure continued for a long time has something to do with it. The tendency to their formation and to consequent fatal cerebral hemorrhage appears to be often hereditary.

FIG. 3.



Miliary aneurism of small cerebral artery (CORNIL and RANVIER).

a, trunk of the artery with fatty granulations, *m*; *c*, perivascular sheath; *b b′*, aneurisms formed by uniform dilatation of the arterial coats; *n*, *h*, blood effused within the perivascular sheath, *c′*; *d d′ f*, capillary branches (30 diameters).

Rupture of veins by mere increase of pressure is not known to occur if the veins are healthy. It has been found experimentally that a tension equal to one hundred times the normal is required to burst the jugular vein of a dog. A vein may be opened, however, by ulceration, as in varicose ulcers of the legs; or by suppuration; or may give way when its structure has already been much altered, as in the case of hemorrhoids.

Rupture of capillaries may, of course, be easily produced by external violence, and occurs also as a consequence of internal pressure. The case in which the latter explanation is most clear is that of punctiform hemorrhages on the serous membranes, seen after death from suffocation, when the veins are greatly distended, and cause pressure in the capillaries which leads to hemorrhage. In most cases it is extremely difficult to distinguish, by the effects, whether capillary bleeding was due to a small rupture or to diapedesis.

Capillary bleeding often occurs in certain specific fevers, as typhus and plague, and in the so-called hemorrhagic form of smallpox and scarlet fever and others, and also in one form of phosphorus poisoning.

In purpura, a disease which consists in hemorrhage in patches, of the skin chiefly, and, less uniformly, of internal organs also, the bleeding appears to be capillary, and is possibly due to diapedesis.

Special Kinds of Hemorrhage.—Special names are given to hemorrhage in particular situations.

Superficial hemorrhages in the skin or other membranes are called *petechiæ*, if they are very small; *ecchymoses*, or *suffusions*, if more diffuse.

Solid tissue soaked through with blood is called *hemorrhagic infiltration*, or, if very clearly limited, *infarctus* or *infarction*.

Bleeding from the nose is *epistaxis;* vomiting of blood from the stomach, *hæmatemesis;* bleeding from the lungs, *hæmoptysis*, or blood-spitting. Blood passed with the urine constitutes *hæmaturia*. Hemorrhage from the uterus is called *menorrhagia* when it is in excess of the menstrual flow; in other cases *metrorrhagia*. Collections of blood within cavities have also received special names, of which one, *hæmatocele*, meaning a collection of blood in the tunica vaginalis, alone requires explanation.

Hæmatoma.—A large mass of blood effused into the tissues or into any cavity whence it is not removed, will, under ordinary circumstances, coagulate. The clot thus formed is sometimes called a *hæmatoma*, or blood-tumor, if it should be at all permanent.

Such masses of blood are sometimes found on the ears as the result of injury to the cartilage and skin, but exclusively in insane persons. It has been supposed that they occur spontaneously, and the question, from its medico-legal interest, has been much discussed; but there can be little doubt that they result from violence in patients whose power of repair are imperfect. They are known as *Hæmatoma auris*. The name *cephalhæmatoma* has been given to an effusion of blood between the cranium and the pericranium in infants at the time of birth, which may remain long fluid, but sometimes becomes covered with a shell of newly formed bone.

Hæmatoma of the dura mater is a collection of blood coagulated in layers on the inner surface of the dura mater, sometimes an inch or more in thickness. It has been ascribed by Virchow to a chronic inflammation of the dura mater—*Pachymeningitis chronica hæmorrhagica*—and is doubtless due to successive effusions of blood mingled with inflammatory lymph.

Blood effused into muscular tissue in consequence of rupture may form a similar tumor-like mass; and the same conditions may occur in other parts.

It should be remembered that these blood-masses are perfectly distinct from tumors properly so called, which will be spoken of hereafter.

When blood is effused from the vessels it will make its way in the direction of least resistance. If the mass of blood is large, it may destroy and lacerate the tissues around, as is seen constantly in the brain, and sometimes, but rarely, in the lungs. In hollow organs it will, of course, fill or line the cavity, and either find its way out by the natural openings or form a cast or mould of the cavity by coagulation. Such moulds are sometimes seen, for instance, in the cavity of the uterus.

In general or parenchymatous hemorrhage, the small cavities will be filled up, as, for instance, the air-cells in pulmonary hemorrhage; the uriniferous tubes in renal. The interstices of the connective tissue being, so far as they admit of it, also filled up, the organ or part is then in a state of *hemorrhagic infiltration*. A part of an organ thus affected is called a hemorrhagic *infarctus* or infarction, or a block, but these are produced by a peculiar modification of causes to be described further on.

Further Changes in Effused Blood.—Generally without forming any such permanent mass as has been described, the blood undergoes a regular series of changes, though a certain part may be carried off at once by the lymphatics.

1. The hæmoglobin diffuses out of the corpuscles into surrounding parts, where it undergoes chemical decomposition, while the stroma of the corpuscles liquefies and disappears. Another portion of the corpuscles and effused pigment is taken by the leucocytes of the tissues, and may be again set free by the disintegration of these, or possibly carried some distance away.

Some corpuscles appear to break down at once, without losing their hæmoglobin, into granular pigmented masses.

As the result of all these processes hæmoglobin is set free, which goes through a series of chemical decompositions ending in hæmatoidin, a dark-red substance in rhombic crystals, or in granular, rust-colored pigment (*see* Fig. 4.) Hæmatoidin is generally thought to be identical with Bilirubin.

(We have introduced, for comparison, a figure (Fig. 5) of hæmin crystals, or hydrochlorate of hæmatin, obtained by the action of acetic acid and chloride of sodium on blood, which is also a derivative of hæmoglobin.)

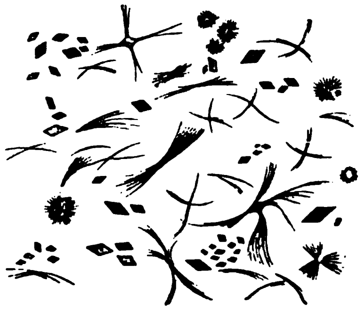
The changes of color seen in a superficial extravasation of blood (or bruise) indicate the stages of this decomposition; and the final brown or rusty stain shows the presence of hæmatoidin or granular pigment.

In internal organs the presence of one or other of these forms may often show that hemorrhage has occurred some time previously; as in the scar in the ovary left by the escape of an ovum at the period of ovulation. Or a yellowish stain in brain-tissue may be the relic of a long antecedent hemorrhage.

It has been shown that the yellow granular pigment is sometimes purely inorganic, consisting of hydrated ferric oxide.

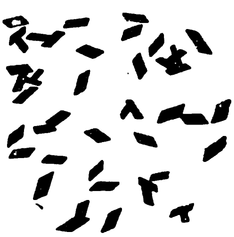
Blood-pigment absorbed by the tissues or lymphatics ultimately leaves the body by the urine, as urinary pigment.

FIG. 4.



Hæmatoidin crystals of various forms (SCHEUBE).

FIG. 5.



Hæmin crystals (SCHEUBE).

2. The fibrin and leucocytes of the clot may entirely liquefy and be absorbed or removed. They may, on the other hand, undergo changes resembling organization, and a fibrous scar is produced, which may be permanent for a long time, and even become calcified.

This change will be more fully described in speaking of the metamorphoses of clots within the vessels (*see* Thrombosis). It is modified, if not entirely caused by the production of inflammation and the concurrence of leucocytes derived from the tissues round the clot.

When the clot liquefies and the tissues around are incapable of contraction, as sometimes happens in the brain, or when it is enclosed in a cavity with thick walls, the liquid remains in the form of a cyst—the so-called *apoplectic cyst*.

General Causes of Hemorrhage.—Besides weakness of the vessels and over-pressure, it has been thought that hemorrhage may be caused by a state of the blood. Especially in the disease scurvy, produced by privation of particular salts, hemorrhages constantly occur. Purpura is another disease in which hemorrhages occur without any obvious local causes, chiefly in the skin, but sometimes in internal organs also. In these cases it is quite possible that an alteration of the blood is the origin of the disease, but it is also possible that degeneration of the walls of the capillaries may be the proximate cause.

Spontaneous Arrest of Hemorrhage.—Bleeding from a large vessel, if very copious, may cease spontaneously, in consequence of the fall in blood-pressure produced by failure of the heart. Besides this, the only causes known to arrest bleeding are, in the case of arteries, contraction of their walls at or above the seat of injury, and, in all kinds of vessels, coagulation of blood.

Tendency to Hemorrhage.—In some persons there is a remarkable tendency to bleed from slight causes, and more especially a deficiency in the power of arresting hemorrhage; so that, after some very slight wound, uncontrollable bleeding sets in. Spontaneous hemorrhages also occur. This remarkable condition, known as hemophilia, or the hemorrhagic diathesis, is generally hereditary, and is far commoner in the male sex than in the female, in the proportion of eleven to one. Careful examination of the vessels has shown no abnormality of structure, and the blood appears to be natural. Except heredity, therefore, no cause for the disease is known.

CHAPTER VII.

THROMBOSIS AND EMBOLISM.

THE word *thrombosis* is applied to the clotting of blood within the living body.[1] This process is essentially the same as that by which blood-clot is formed outside the body, or after death; but since the blood in general preserves its fluidity within the bloodvessels during life, there must be some special cause or causes to produce thrombosis. To understand what these causes are, we must first consider what conditions maintain a fluid state of the blood in the normal circulation.

Without discussing the cause of coagulation, it is clear that this does not take place so long as the blood is in motion and the walls of the vessels containing it are living and intact. If the vessel-wall, whether of heart, vein or artery, be injured so as to destroy its vitality, coagulation sets in. If the blood be stagnant at any part for a certain time, the same result follows; not, it would seem, from arrest of motion alone, but because this interferes with the nutrition of the inner coat of the vessels.

The influence of the normal walls in preserving fluidity is also shown indirectly by the fact that when the blood leaves the vessels (in hemorrhage) and passes into any cavity of the body or among the tissues, it always coagulates, though not always immediately. Now, it would evidently amount to the same thing if a portion of tissue should gain admittance within the vessel. This is what actually sometimes happens in the case of cancer and new-growths, which may grow into a vein by perforating the wall, and when they do so produce a thrombus inside. If pus or other inflammatory products come in contact with the blood inside vessels, they also produce coagulation.

The same result occurs with necrotic masses, such as those derived from tubercle, etc. The effect of foreign bodies, such as ligatures, needles, etc., in causing coagulation is well known. It is more marked in proportion as the surface is rough, smooth glass having little effect. Various chemical agents (acids, salts, etc.), injected into vessels, are known to cause coagulation, and so does the electrolytic current. Generally, the contact of any substance other than the normal wall of the vessel, determines a precipitation of fibrin on its surface.

It is important to remember that a clot once formed acts as a foreign body. Hence the tendency of a thrombus to extend. If the clot originally formed be called the *primitive* thrombus, the subsequently formed clot is called *secondary* thrombus.

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[1] The English words *curd* or *clot*, *curdling* or *clotting*, the Latin *coagulum*, *coagulatio*, the Greek θρόμβος θρόμβωσις (*thrombos*, *thrombosis*), precisely correspond in meaning, being used both of milk and of blood: but the Greek words are, for convenience, used in the special sense pointed out above.

We may sum up the causes of coagulation of blood within the vessels thus:

1. Stagnation, or arrest of circulation, which acts indirectly.
2. Injury, or necrosis, of the inner coat of the vessels, directly.
3. Introduction of tissues or materials from other parts of the body, or of foreign substances into the vessels.
4. Secondary extension of the clot from clot already formed.

It may be thought that a certain condition of the blood is also a cause of coagulation. After severe fevers, as typhoid, extensive thrombi are sometimes formed in the veins, and in conditions of exhaustion and wasting from fatal diseases the same occurs. This has been called cachectic thrombosis (marantic thrombosis, Virchow), and is a condition of much importance. There are, however, doubtless several causes which coöperate in these cases. The circulation is retarded, from weakness of the heart. The tissues generally are badly nourished, and this defective nutrition is particularly liable to affect the inner coat of vessels. Moreover, in several of such diseases micro-organisms are present, which probably have some effect in favoring coagulation. Admitting that these conditions make the blood more readily coagulable, we still have to find the local determining cause. Such causes are:

1. *Stagnation or stoppage of blood; chiefly seen in the veins and the heart.*—In veins pressed upon from outside by any cause, the current may be completely arrested; and the blood will sooner or later coagulate, forming a *thrombus*. This is most often seen in the deep veins of the pelvis or abdomen. It may happen in the female sex during pregnancy; and must often occur from other causes, since old, calcified thrombi are frequently found *post mortem* in the ovarian plexuses and neighboring veins. In the other sex the prostatic plexus shows a similar liability, and in both the hemorrhoidal veins. It is easy to see that accidental mechanical causes may lead to the same result in other systemic veins. In the portal system and in the pulmonary veins, thrombosis from this cause alone is not common. General weakness or slowness of the circulation is thought to be a cause of venous thrombosis, but it is not quite clear that it is so, unless there be a local cause also.

The way in which stagnation of blood leads to coagulation is, that the inner coat of the vein (which is nourished by the circulating blood) is impaired in its nutrition, as we have before seen to be the case even with venous hyperæmia. It then acts upon the blood like dead or foreign matter.

In the arteries, the circulation being so much more energetic, coagulation from stagnation is evidently not likely to occur.

In the heart we find that a very feeble circulation strongly predisposes to coagulation, and that thrombosis may be produced there without any other causes, so far as we know, being concerned. When, from any chronic disease of the heart, its contractions become very feeble, the chambers are imperfectly emptied, and a portion of blood will tend to stagnate in those parts of the auricles and ventricles where the movement is less vigorous. This will be the case in the apices of the ventricles and the appendages of the auricles. For some reason, the left ventricle and right auricle are most often affected.

In these parts we may find masses of fibrin adhering to the walls. Sometimes the clot assumes a globular shape, still attached to the walls, or may even be detached all round. These masses have received various names, as cardiac polypi, globular vegetations, etc., and were at one time attributed to endocarditis, with which they have nothing to do. The globular thrombi are generally softened and sometimes quite liquefied, so that they may contain a pulpy matter resembling pus in appearance.

These clots are generally formed some time before death, as is seen, on post-mortem examination, by the changes they have undergone. There is, therefore, generally no difficulty in distinguishing them from the clots resulting from coagulation of blood in the heart after death.

The distinction is more difficult if, as sometimes happens, clots are formed immediately before death, when the heart's action is beginning to fail. Here the clot will not have undergone any changes, and we can only be guided by the evidence of the clot having been formed while the blood was moving, or after the circulation had stopped. This is an important but difficult point.

Distinction of ante-mortem clots (thrombi) and post-mortem clots in the heart.—Clots formed some time (days or weeks) before death, will be more or less adherent to the walls and show some changes of color and consistence, which will be described afterward.

Those formed after death are either soft and black, with the corpuscles and fibrin quite uniformly mingled, or else they show some separation of fibrin from the other constituents. These two cases correspond to the two ways of coagulation seen in blood out of the body. In the latter case the fibrin will be seen to occupy the highest position, as the body lies (that is, in front of the two ventricles, and the commencement of the great vessels), while the red corpuscles gravitate to the lowest part. This is exactly the way in which the blood constituents arrange themselves in a bleeding-basin, if separation of fibrin takes place; and hence this may be called the bleeding-basin clot, which is always formed *post-mortem*, and is not a thrombus.

In the case of clots forming during the last hours or days of life, there may also be a separation of fibrin, but this will be arranged irregularly, attached to the walls or musculi papillares, not distributed according to the action of gravity. Strings of fibrin may also extend along the aorta or larger arteries. Unless these characters, which show that the fibrin separated while the blood was in motion, are clearly marked, it must be supposed that the clot was formed *post-mortem*. Cases have occurred in which this coagulation in the heart before death has been diagnosed during life, and confirmed by post-mortem examination.

2. *Thrombosis from changes in the walls.*—In veins this is a common cause. Inflammation of the walls, whether caused by a wound, or by extension from an inflamed part, produces local coagulation. Formerly this was thought to be the universal process, and all of what is now called thrombosis was called phlebitis; but this was a mistake, since thrombosis may occur independently, and may produce inflammation of the walls. In other words, phlebitis is one of the causes of thrombosis, but thrombosis may also be a cause of phlebitis.

Inflammation is particularly liable to affect the veins, if the original inflammation is of an infective or specific kind. Hence thrombosis is very likely to occur in the case of unhealthy wounds.

In the heart local endocarditis, when it affects the walls (not a common event), produces coagulation on the inflamed patch.

In arteries change in the inner wall is the commonest cause of thrombosis, but this is a matter of degree; and if the circulation be vigorous, even a considerable change of surface will not necessarily produce coagulation. When the circulation is sluggish this is more often seen.

In atheroma of the aorta, calcareous plates are often found which, in some cases by absorption of the inner coat, come into contact with the blood-current, and may cause deposition of fibrin upon them. The same may occur, though rarely, in smaller arteries, and cause complete obstruction of them, the consequences of which may be—for instance, in the arteries of the brain or the heart—very important or even fatal. The clot thus formed may extend in either direction. This process is with difficulty distinguished from the results of embolism, explained below.

Extensive thrombosis of the pulmonary artery is sometimes seen, where it may be doubtful whether this was the original process or whether it was caused by embolism (*see* below).

3. *Thrombosis from entrance of some foreign substance into the vessels.*—This process is important only in relation to veins.

Cancer or other new growth may sometimes grow into a vein and produce a thrombus. By extension of the growth into this a *cancerous thrombus* is formed, which may grow on continuously or become detached and carried to a distance. Chondroma, lymphoma, and other tumors may, rarely, act in the same way.

A new growth in the heart may produce similar results.

Pus sometimes perforates the wall and enters a vein, when it produces a clot. This was at one time thought to be a common process, and to be the cause of the disease called pyæmia. It is now known to be of very rare occurrence, but unquestionable instances have been seen by the writer.

What more generally happens is that inflammation of the vein is produced by the neighborhood of suppuration, and thus a thrombus is formed. But this thrombus will become infected with any specific poison which is contained in the pus. Thus a foreign substance, viz., the microörganism or whatever else constitutes the specific virus of the pus, may enter the vein.

This may possibly be conveyed by migratory cells, or may itself penetrate the wall and enter the clot.

The production of thrombi containing specific infective substances is a most important and dangerous process. By this means, just as in the case of cancer, a specific disease may be distributed over the body.

Thus an unhealthy wound, containing septic bacteria, gives rise, by thrombosis of the neighboring veins and subsequent changes, to the general disease *pyæmia*.

The tubercle poison, and possibly that of syphilis, are sometimes distributed in the same way.

4. *Production of thrombus by extension; secondary thrombosis.*—A clot once formed has a tendency to enlarge, by coagulating the blood next to it. In this way the coagulation which begins at one side of the inner wall spreads until the vessel is blocked. When this occurs the whole column of blood behind, in the vein itself and its tributaries, is arrested, and will also coagulate. The thrombus may also extend forward with the blood-current until this is stopped, and even further if the vein do not collapse.

Thus coagulation may extend to parts quite remote from the primitive thrombus. For instance, let a thrombus be formed in a small tributary of the internal iliac vein. It will creep along until it reaches the internal iliac trunk and projects into this. A secondary thrombus is formed, which spreads up to the junction with the external iliac. The latter will become blocked, and the thrombus extend down the femoral to the principal veins of the leg. This is nearly what occurs in the disease called phlegmasia alba dolens, where coagulation starts in the uterine veins, and causes pain, swelling, etc., of the leg.

Consequences of Thrombosis.—That when a vein is obstructed by thrombus the parts behind the obstruction are affected in the same manner as if the vein were stopped in any other way—*i. e.*, show hyperæmia, engorgement, œdema—need hardly be pointed out. Other consequences depend upon portions of the thrombus becoming detached and carried onward by the blood-current to the heart or other vessels, as will be explained when the changes in thrombi have been spoken of.

The consequences of obstruction of arteries by thrombus are the same as those of obstruction by other causes, and will be afterward discussed.

Structure and Metamorphoses of Thrombi.—Thrombi are spoken of as (1) parietal and (2) obstructive, according as they are attached to the wall of the vessel or occupy its whole lumen.

The one kind may, of course, pass into the other, but the structure of those which are at first parietal is different from that of those which are formed by coagulation of the whole column of blood in a vessel.

1. Parietal thrombi are always formed of successive layers. The first layer (as Zahn has observed during life in the transparent parts of frogs) is formed of leucocytes with a little fibrin; on this another layer is deposited, and so on. For some reason not understood the successive layers are often different in color, some consisting entirely of leucocytes and fibrin, others containing red corpuscles also, produc-

ing an appearance like the structure of an agate. This laminated structure is traceable to the last in such thrombi, and is often obvious to the naked eye, for instance in the layers of clot inside an aneurism. Some parietal thrombi are almost wholly composed of fibrin and leucocytes, and are known as "white thrombi." Some layers may be transparent or hyaline, but generally there is a large quantity of a finely granular substance known as molecular fibrin.

A different explanation has lately been given of the formation of white thrombi. It is said that the leucocytes take no necessary part in their formation, but that they originate in the "blood-plaques" or elementary blood-corpuscles which have been lately much studied. According to the observations of Bizzozero, substantially confirmed by other investigators, the first result of injury to the wall of a blood-vessel or the introduction into its cavity of a foreign body such as a thread, is the deposition of a mass, not of leucocytes as formerly supposed, but of blood-plaques. Osler has found even large masses of white thrombus to be chiefly composed of these elements, the outer parts showing them in a perfect state, the inner part consisting of a granular mass resulting from their disintegration. Bizzozero holds that the blood-plaques are the essential agents in the precipitation of fibrin which properly constitutes coagulation. Others think that there is no connection, and the question is not yet decided.[1]

2. Obstructive thrombi consisting of the whole mass of the blood will at first precisely resemble ordinary clots formed out of the body, but undergo certain changes.

These changes are:

In the first two or three days the thrombus becomes firmer and drier from loss of the serum squeezed out of it in contraction. Next it becomes somewhat adherent to the wall of the vessel. Later on the blood-pigment diffuses out of the corpuscles, and the whole clot becomes tinged of a reddish-brown color from altered hæmoglobin or hæmatoidin. This is, however, absorbed, and the clot becomes partly decolorized, especially in the central portions. This loss of color is good evidence of the age of a clot.

What may be considered the natural or healthy end of this process is the so-called "*organization of the thrombus.*" It becomes gradually replaced by a mass of connective tissue, which either converts the obliterated vessel into a fibrous cord, or else becomes channelled and allows it to become pervious again.

There has been much discussion as to whether the connective tissue is formed out of the elements of the clot or by outgrowth from the walls of the vessel.

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[1] I have had no opportunity of testing these observations as regards thrombosis, but the blood-plaques are described and discussed further on in speaking of the variations in the corpuscles of the blood. For further references see Schimmelbusch, Virchow's Archiv, vol. ci. p. 201; Eberth, *ibid*, vol. ciii. p. 39; Osler, British Medical Journal, 1886, i. p. 807.

The general conclusion is that the thrombus itself plays a passive part, and that the new tissue is an outgrowth from the endothelium of the vessel, which becomes vascularized from the vasa vasorum. The author's own observations are entirely in favor of this view. The clot may be seen pushed aside and replaced by a transparent, gelatinous-looking tissue directly continuous with the thickened *intima*. If this be true, there is no organization, properly speaking, of the thrombus. It is, however, not impossible that some elements of the thrombus, viz., the leucocytes, may be taken up into the new growth.

Softening of Thrombi.—This, which is the other possible termination of the metamorphosis of the clots, is a process of great importance. It begins, like the other process, with diffusion, followed by absorption of blood-pigment. Softening begins in the central and decolorized portions of the thrombus, where the fibrin is liquefied and a pulpy or creamy substance produced. Under the microscope this is found to be granular matter with shrivelled and degenerated leucocytes. Rarely the number of these cells is so great as to produce an appearance something like pus; hence the process was at one time called suppuration, and thought to show inflammation of the vein. But the puriform matter was shown, first by Gulliver and afterward by Virchow, to be softened fibrin and blood-cells. Sometimes it contains septic or putrid substances, if derived from tissues containing such matters. Generally, though not always, the walls of the vein are at the same time thickened and inflamed.

Softening is particularly well marked in thrombi of the heart, and appears to be the constant process there. It is doubtless favored by the circumstance that the thrombus is soaking in the fluid blood. This process also takes place more regularly, and perhaps more rapidly, when the temperature of the body is raised by fever.

The result of softening is, that portions of the thrombus, either in the form of a pulp or of solid fragments, are likely to get into the circulation.

The effects thus produced will be various:

The softened matter may pass into the blood without producing any injurious symptoms, the only result being that the channel of the bloodvessel is opened up. This is more likely to occur in thrombosis of an artery than of a vein.

A fragment may be carried into some vessel which it will obstruct; it is then called *embolus*.

This matter may contain a septic or infective poison. It will then produce a general disease, and also set up suppuration or necrosis at the spots where it ultimately becomes lodged.

Fragments of thrombi may doubtless be detached by movement or by some mechanical accident, without softening, and be carried off by the blood stream. Thus we sometimes find large and firm masses of a venous clot in distant parts.

These results depend on the process called Embolism, which must now be described.

EMBOLISM.

This name, derived from the Greek word *embolus* (ἔμβολος), meaning a *plug*, denotes the plugging or stopping up of a bloodvessel by a mass brought by the blood and too large to pass through it. This process can only occur in the systemic or pulmonary arteries, or in the branches of the portal vein, and, with some modification, in capillaries.

The obstructing plug or embolus may be, as shown, a fragment of a thrombus. Such fragments, derived from the systemic veins, will be carried to branches of the pulmonary artery; if derived from the left side of the heart, or the pulmonary veins, will obstruct some systemic artery; if derived from factors of the portal vein, will go to branches of that vein within the liver.

Other substances which may act as emboli are fragments of vegetation from the valves of the heart; parasites; portions of new growths which have entered the veins, etc., without speaking of foreign bodies introduced experimentally.

Fat may, under certain circumstances, act as an embolus, and so perhaps may air introduced into the veins.

Sometimes finely divided substances will pass through the pulmonary capillaries and become arrested in the systemic circulation.

Emboli may be classified as *simple* or mechanical; and *specific.*

The former produce merely the effect of obstruction. The latter give rise either to new growth (cancer, etc.) or to inflammation at the point where the vessel is obstructed.

Simple obstruction of an artery by an embolus is generally recognized during life by the suddenness of the symptoms. The further consequences depend on the part obstructed. In most cases the obstructing mass is increased by the extension of thrombus from the embolic mass. This arises from the fact that a column of blood, both in front of and behind the embolism, is brought to a state of rest, and coagulates. It would seem, in some cases, that partial obstruction of the artery, by merely retarding the current, is even more effectual.

The embolus, for obvious reasons, is most frequently arrested at the bifurcation of an artery, where it can go no further, and the secondary thrombus may extend from this point into the branches of the artery. In such a case the secondary thrombus may be a much more conspicuous object than the embolus which gave rise to it, and the latter being enveloped in fresh clot, minute research is required to find the origin of the mischief. The distinction from arterial thrombosis will here be difficult, and opposite opinions may be arrived at by different observers with respect to the same specimen.

The following actual cases of embolism may be taken as typical *instances:*

1. A woman some days after childbirth is taken with sudden dyspnœa and cardiac syncope, which are rapidly fatal. On opening the heart we find in the right ventricle a piece of firm thrombus some

two inches long, and as large as a cedar pencil, which had obstructed the pulmonary artery and caused death. In the internal iliac vein we find a thrombus with a broken end, which exactly fits one end of the mass found in the heart, so that the latter was evidently broken off from it. The detached thrombus, in the case related, showed also the imprint of the valves of the vein. This is *pulmonary embolism.*

2. A patient with aortic valvular disease is suddenly seized with right hemiplegia and aphasia and other symptoms showing affection of the part of the brain supplied by the left middle cerebral artery. After death, a few days later, that artery is found blocked by an irregular fibrinous mass, which has been arrested at the bifurcation of the vessel. The corresponding brain substance is in a state of acute softening. On looking at the aortic valves, vegetations are found on them which precisely resemble the plug stopping up the cerebral artery. This is *cerebral embolism.*

3. In the same disease there may be sudden and painful obstruction of one femoral artery; the limb becomes cold, pulseless and ultimately gangrenous. The artery is found to be blocked (probably at the giving off of the profunda), by a mass like those on the aortic valves.

4. A patient with mitral regurgitant disease has repeated hæmoptysis, with cough, etc. After death we find several branches of the pulmonary artery blocked with fibrinous plugs; while softened thrombus is found in the right chambers of the heart. The lung tissue connected with the blocked arterial branches is a solid red or yellowish mass; the so-called hemorrhagic infarction or *infarctus.*

It thus appears that the results of blocking an artery may be very different in different cases; the results (not to speak of sudden death from blocking of the pulmonary artery); may be thus classified:

1. If the main artery of a limb be blocked, the anastomosis may be perfect enough to restore the circulation after a time, so that no permanent effects follow. If the anastomosis be insufficient we get, in external parts, gangrene.

2. If an artery going to an internal organ be blocked there will in many cases be sufficient lateral anastomosis to restore the circulation. But if it be a "terminal artery"—that is, a branch which has no lateral communication with other branches—the supply of arterial blood is, of course, cut off; and certain results follow.

3. Even if there be no anastomosis, gangrene does not occur unless the part be somehow in communication with the air. The result is either:

(*a*) Rapid necrosis, *i. e.*, softening, as seen in the brain, an organ which cannot bear even temporary cutting off of its nutrition This is best seen in the middle cerebral artery, because it lies beyond the circle of Willis and has no arterial anastomosis.

(*b*) Slower necrosis or wasting, as may happen, for instance, if the main renal artery be obstructed.

(*c*) The part supplied by the artery may become engorged, and even diffuse hemorrhage occur. This constitutes a hemorrhagic infarctus, or hemorrhagic block.

Such blocks are formed only in the lungs (branches of the *pulmonary* artery), the spleen, the kidneys, retina, rarely in the intestinal canal.

In these organs the branches formed by subdivision of the main artery are terminal arteries; hence the portion supplied by each branch forms an isolated territory.

We might expect that this portion would be anæmic if its artery be blocked; how then does it come to be engorged and hemorrhagic?

This is a difficult question. There can be no doubt that the part becomes filled with blood, which stagnates there; and this blood can only come from one of two sources, either by regurgitation from the *veins*, or by slow infiltration from *capillaries* which communicate with the arteries of adjacent territories. The first explanation is Cohnheim's, and is very plausible, but is contradicted by experiments which show that the same result follows even if the venous as well as the arterial branch be blocked. On the other hand, the capillaries may bring blood from adjacent parts, especially if (as is always the case) the blocks are situated near the surface. Then the blood-supply of the covering of the organ (pleura, capsule of the kidney, etc.) comes into play, when the onward driving force of the artery is suspended. Moreover, it should be remembered that such infarctions nearly always occur in cases of obstructive heart disease, when there is venous engorgement of the pulmonary circulation, and of the whole venous system. By whatever means, an engorged condition is established, though not immediately. It takes time—probably two or three days at least—since if the artery be blocked immediately before death, this result does not follow (I speak from personal observation).

Then other changes follow:

Hemorrhage by diapedesis occurs through the whole mass of the block. This occurs because the walls of the vessels have been weakened and necrosed by being deprived of arterial blood. The red blood-disks more especially (as in venous hyperæmia) leave the vessels. This is shown often during life by external bleeding—*e.g.*, hæmoptysis or hæmaturia; and may be seen in the retina by the ophthalmoscope. Necrotic changes follow. The block becomes decolorized, as a thrombus does; its central parts become yellow and crumbling, or break down to a pulpy mass resembling pus. But suppuration does not occur unless the embolus has brought some infective poison. There is active hyperæmia in the outer parts, forming a brightly injected zone and increase of fibrous tissue, so that something like a capsule is produced. In the end a depressed fibrous scar results, which is permanent in the spleen or kidney, but in the lung becomes almost or quite imperceptible, This series of changes may be gone through in the kidney in about six weeks.

The above description applies to lung, kidney, spleen, and retina (*mutatis mutandis*). In the intestine the same condition (producing hemorrhage from the bowels) may occur if, beside the blocking of one branch of the mesenteric artery, we have obstruction by thrombosis of the anastomotic loops, which would otherwise restore the circulation, as I have had an opportunity of observing. The above described changes occur whatever be the nature of the obstructing mass—a fragment of fibrin or any other substance.

On consideration, we see that emboli in the pulmonary circulation must be derived from the systemic veins or from the right side of the heart; emboli in the systemic arteries are mostly derived from the heart, consisting of fragments of diseased valves, or of fibrinous deposits, called vegetations, upon them; or else possibly from thrombi of the pulmónary veins. It is also possible for matters such as the products of atheroma, or deposits of fibrin, to be carried from larger into smaller arteries, and there to form emboli. In the portal vein, emboli are derived from its factors.

Aneurism from Embolism.—In solid organs the obstructed arterial branch is probably seldom reopened. In cerebral arteries and some others this is possible, but the wall of the artery will be permanently injured, and a curious result sometimes follows. A local dilatation or aneurism may be formed; and thus embolism may be a cause of small aneurisms, otherwise unexplained, of the cerebral arteries. It is possible the same may happen in other arteries not supported by solid tissue—*e. g.*, in the mesenteric, as appeared probable in one case which came under the writer's observation.

Infective Embolism.—If, however, the fragment brought from a thrombus contain the infective poison derived from a wound or elsewhere, it will not only produce some degree of infarction as above described, but will also excite active inflammation. Hence, instead of a simple block, an abscess results. These pyæmic abscesses, formerly called *secondary deposits* (*i. e.* of pus), have, in the lungs, a certain resemblance to hemorrhagic blocks, but differ in showing pus and other signs of active inflammation. In other parts, as the liver, they are more like simple abscesses.

Thus thrombosis and embolism are the machinery by which the poisons of pyæmia, etc., are distributed through the body. It is probable that the fever and blood poisoning induced by the general disease also modify the local process. In the same way these processes may serve as the machinery for the distribution of new growths.

Capillary Embolism.—Particles of various kinds which are too small to obstruct visible arterial branches may yet be too large to pass through capillaries. They then produce what are called capillary embolisms. But it is well to remember that under this name is included obstruction of minute arterioles, which naturally often happens simultaneously and from the same cause.

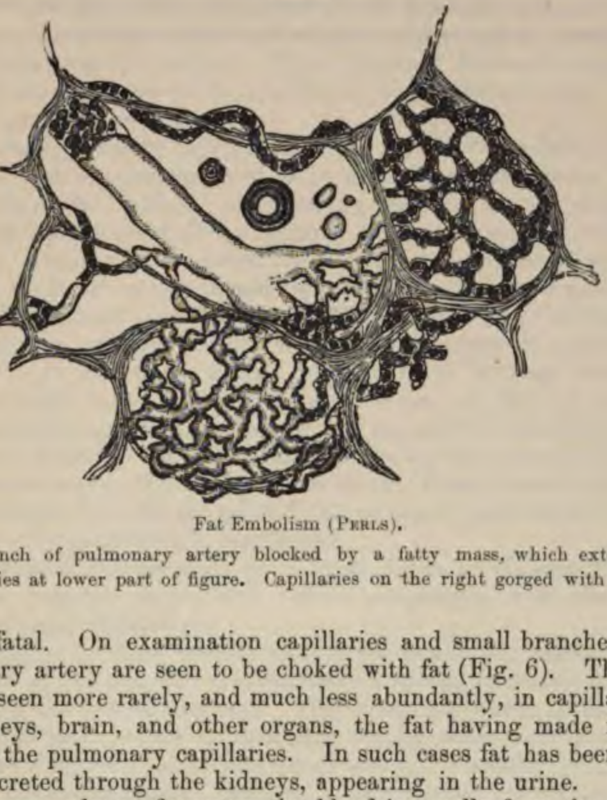
A capillary, being of uniform diameter, ought to allow anything to pass which is small enough to enter it; but doubtless obstruction is often caused by the adhesive nature of the obstructing substance, or because it produces some change in the capillary wall.

Capillary embolisms may be produced by solid or liquid substances, and perhaps even by air.

In many febrile conditions, capillaries are found blocked by masses of leucocytes. In infective diseases, groups of micrococci and possibly bacilli, in addition to their specific action or perhaps in consequence of that, cause obstructions in capillaries. Capillary embolism may also be a consequence of one form of endocarditis.

Fat Embolism.—Fatty matters contained in the blood have some difficulty in passing the pulmonary capillaries. When present in quantity, they cause extensive obstruction, with dyspnœa, etc., which may be fatal. On examination capillaries and small branches of the pulmonary artery are seen to be choked with fat (Fig. 6). The same may be seen more rarely, and much less abundantly, in capillaries of the kidneys, brain, and other organs, the fat having made its way through the pulmonary capillaries. In such cases fat has been found to be excreted through the kidneys, appearing in the urine.

FIG. 6.



Fat Embolism (PERLS).

Small branch of pulmonary artery blocked by a fatty mass, which extends into capillaries at lower part of figure. Capillaries on the right gorged with blood.

The source whence fat enters the blood is usually from the marrow of bones after severe fractures or in osteomyelitis, but it is said to have been also derived, in some cases, from wounds of adipose tissue.

When it affects a large portion of the pulmonary circulation, sudden death may result.

Air Embolism.—It has long been known that the entrance of air into the veins, which may happen in operations on the large veins of the neck, etc., is a dangerous and possibly fatal occurrence. The bad effects have been thought to depend on obstruction of the pulmonary capillaries by air-bubbles, but seem rather to be due to accumulation of air in the right ventricle, which contracts ineffectually upon the air, and does not propel the blood.

Pigment embolism is said to occur in intermittent fevers when the blood becomes loaded with pigment, and to cause obstruction of capillaries and small arteries. But it is probable that in these cases the pigment is contained in cells.

Parasitic Embolism.—Small animal parasites may get into the circulating blood and block up a vessel which they are too small to pass through. This process is common in certain animals—*e.g.*, a worm called strongylus armatus lodges in the mesenteric arteries of horses, where it produces small aneurisms. But such an occurrence is unknown, or excessively rare, in the human subject.

CHAPTER VIII.

PATHOLOGICAL RELATIONS OF BLOOD-PRESSURE.

THE varying amount of pressure exerted by the blood upon the walls of the vessels containing it, is so important a factor in many pathological processes that it is desirable to give a short summary of what is known on this subject. The pressure of fluids on vessels containing them requires to be considered as hydrostatic and hydrodynamic pressure respectively.

Hydrostatic pressure depends upon the weight of the fluid, without reference to its movements, and is at any point proportional to the depth below the surface, while acting equally in all directions. Hydrostatic pressure is of no account in the human body except in the veins, since in the arteries the movements impressed upon the blood by the heart are so considerable that the pressure due to the weight of the blood is relatively unimportant and may be neglected.

Hydrostatic pressure in the veins only becomes of pathological importance in the veins of the lower part of the leg, which are exposed to the internal pressure of a column of fluid of a height equal to the distance from the foot to the entrance of the inferior vena cava to the right auricle, where, at least during the auricular diastole, the pressure is negative. The valves of the veins, though they prevent backward flow, do not take off this pressure, since when they are open the column of fluid is continuous.

The effect of this pressure is in many cases to produce irregular dilatation (varicose veins) and venous congestion, with the consequences already pointed out.

In addition to these special morbid conditions, all diseases of the lower part of the legs and the feet have a special character imparted to them by the venous pressure. This is especially seen in inflammations of the skin, which in this part usually show more congestion than elsewhere, have a deeper color, and are especially liable to be followed by pigmentation. Dropsy, from impeded circulation, as in cases of heart disease, is of earlier occurrence, and usually more intense in these parts than elsewhere.

Probably the same cause partly determines the special incidence of gout in the feet, where, the blood-current being delayed, deposition of urates is more likely to take place. The association of an affection of the veins with gout in the feet is sufficiently common to have suggested the hypothesis that phlebitis is a (local) cause of gout. But, after all, gout begins in the joints.

Hydrodynamic Pressure.—The pressure exerted by the moving blood upon the walls of the vessels is a varying one, and modified by four chief factors—(1) variations in the volume of the blood; (2) variations in the capacity of the vascular system; (3) facility of outflow of the blood from arteries into capillaries; (4) the force of the heart.

To understand the first cause of variation, we must leave out of consideration for a moment the action of the heart, and suppose the blood to be either at rest or moving uniformly along the vessels. It will then exert a certain pressure on the walls of the vessels, which pressure is a force acting uniformly in all directions. The resistance of the vessel walls must, by hypothesis, be a force equal and opposite to this. Now, since blood, like water, is an inelastic fluid, there would, if the vessel walls were perfectly rigid, be no room for variations in the volume of blood. But the vessel walls are distensible and also elastic; so that they can both hold varying amounts of blood, and also exert a tension proportional to the varying force of the blood-pressure. Hence blood-pressure and tension in the walls of vessels are corresponding terms. We can reproduce the conditions if we force water into a thin India-rubber tube of which one end is closed, or partially closed, so that the passage of fluid is retarded; the India-rubber will be distended, its elasticity brought into play, and there is a certain degree of tension in the India-rubber with corresponding fluid pressure in the water.

The blood vascular system as a whole represents such an India-rubber tube which is slightly over-distended—that is, distended so far as to bring its elasticity into play to a certain extent. This elasticity is most marked in the arteries; veins and capillaries possessing very little, or in some parts, perhaps, no elasticity.

If now, the volume of the blood be increased by the formation of more blood, or by the absorption of more fluid, as must always happen after a meal, or after ingestion of large quantities of liquid, the blood-pressure and corresponding tension of the walls will rise. The increased blood-pressure will continue until the capacity of the vascular system is enlarged. This enlargement is brought about in life by relaxation of the muscular fibres in the arteries under the influence of the vaso-motor nerves; and by direct enlargement of the veins, which, being perfectly elastic, give way to increased pressure. The capacity of the capillaries varies under such circumstances very little. There may also be an opening up, or at least very great enlargement, of collateral channels not used before.

In this way the vascular system may make room for greatly increased volumes of blood without any permanent rise of pressure.

This condition can hardly be imitated experimentally, but would be paralleled if we imagine a larger tube substituted for that with which we began the experiment. It is obvious that a larger amount of fluid could be contained without increased tension.

Now, on the other hand, let us suppose the volume of the blood to be diminished, either by a large hemorrhage, or by loss of water through copious and rapid diarrhœa or profuse perspiration.

In this case there will be an immediate fall of blood-pressure, and corresponding loss of tension in the walls (like an India-rubber tube not containing water enough to keep it distended), and this will last until compensation is effected by a diminution in the capacity of the containing vessels. Their capacity will be diminished by contraction of the muscular walls of arteries under the influence of the vaso-motor nerves, and perhaps also by contraction—partly muscular, partly fibrous—of the walls of veins, till at length the whole vascular system will have contracted down upon the diminished volume of blood, and the pressure (and tension) may be as high as before. This mechanism is set in action (according to Cohnheim) by the fact that anæmia is a direct stimulant of the vaso-motor centre in the medulla oblongata. Hence loss of blood, especially if it be sudden, causes stimulation of this centre, and contraction of all the arterial muscular walls controlled by the vaso-motor nerves. These conditions are not imaginary. The volume of the blood is perpetually fluctuating, being increased by ingestion of food and drink, diminished by egestion of feces, urine, and sweat; and these fluctuations would produce more permanent changes in blood-pressure if they were not equalized by the compensatory mechanism above referred to.

It should be remembered that the fluctuations in the volume of the blood are also compensated by increased transudation in the case of excessive, and increased absorption of fluid in the case of inadequate volume. But this is a slower process than the compensation by changes in the capacity of the vascular system. The latter is an affair of minutes or even seconds (experimentally); the former, of hours or days.

Blood-pressure as Influenced by the Capacity of the Vessels.—If the capacity of the vascular channels be diminished without change in the volume of blood, as will happen if any large channels are closed, or if the muscular walls of the vessels either generally or in any large division of the system contract, the tension or blood-pressure will increase till it is equalized, either by an enlargement of the vascular system in another direction, or (what can only happen comparatively slowly) a diminution in the mass of the blood by transudation of water. Conversely, if the capacity of the vascular system be increased, as, for instance, by a relaxation of the muscular coats of the vessels, either generally or over a considerable part of the system, the tension is relaxed, and the blood-pressure falls. But it will rise again if another part of the vascular system contract in a corresponding degree, or if the mass of the blood be again increased by the absorption of water. Perfect compensation is possible in either of these directions. Practically the amount of blood sent into the splanchnic vessels, and thus into the abdominal viscera, is one of the most important conditions regulating the amount contained in the rest of the vascular system. It is calculated that these vessels may be dilated so as to contain all the blood in the body; and in the condition of shock they do contain so much as to render the other arteries and veins almost empty, with a corresponding fall of pressure.

Limitation to Arterial Blood-pressure.—The changes just mentioned are quite possible, and theoretically must have the effect ascribed to them; but they are practically of no great importance, because we cannot recognize the pressure in, or the capacity of, the vascular system as a whole. Our knowledge is almost confined to changes of calibre and pressure in the arteries. But it does not follow that these are accompanied by corresponding changes in the veins. It is rather probable that there is a converse relation, so that when the arteries are contracted the veins are dilated, and *vice versa*. By blood-pressure is generally understood arterial tension.

We shall, therefore, now confine ourselves to the consideration of modifications of *arterial* blood-pressure as produced by changes in the capacity of the *arterial* system. For though temporary fluctuations in the volume of the blood will influence the arterial blood-pressure temporarily, for reasons stated above these disturbances are speedily compensated, and hence the chief practically important condition is the varying capacity of the arterial system.

In order to get a precise conception of the way in which this acts, let us suppose—what is a common occurrence—the ligature of a large artery, such as the femoral, or the application of Esmarch's bandage to the limb, by which a notable portion of the arterial system is cut off without any diminution in the mass of the blood. It would seem as if the tension in the arteries of the rest of the body must be immensely raised. We think of the danger of ruptured vessels and so forth. But what is the case? There is indeed a rise of pressure, but only a temporary one. After a few minutes or even (in experiments) some seconds, the blood-pressure falls to what it was before. What is the explanation of this result? It clearly cannot be due to any corresponding reduction in the volume of the blood, as, for instance, by increased transudation. Such a process could not be effected so rapidly. There are only two possible explanations. One is that the relative excess of blood for which there is not room in the diminished arterial system may be stowed away in the veins. This is not impossible; but even in that case there is reason to believe that though there would not be more blood in the arteries their tension would be raised.

The only alternative explanation seems to be that the capacity of the remaining portion of the arterial system becomes increased, and the tension lowered in a corresponding degree. To understand this we must remember that the capacity of the arteries, being controlled by their varying calibre, is constantly fluctuating. The smooth muscle-fibres in their walls are contracting or dilating continually in response to various stimuli. These changes are doubtless most marked in the smaller arteries or arterioles, because their walls are relatively more muscular; but wherever smooth muscular tissue exists it is subject to the same laws, and we can only understand these conditions by regarding the arterial system as a whole, not selecting one portion for exclusive attention. We have then to inquire what is the normal regulative or adaptive mechanism influencing the capacity of arteries.

Normal Regulative Machinery of Arteries.—Under normal conditions the capacity of the arteries depends upon their varying calibre, as influenced by the contraction of the smooth muscle-fibres in their walls. These muscles are controlled through the vaso-motor nerves by a nerve-centre (the vaso-motor centre) in the medulla oblongata, and locally by centres in the sympathetic ganglia of different parts, and probably also by centres in other parts of the spinal cord, acting through the vaso-motor nerves.

The function of the vaso-motor centre is to produce a vascular tone, or a state of contraction, in the different parts of the arterial system. If the centre be stimulated, this tonic contraction is increased. Such a stimulation is usually reflex, depending on a stimulus transmitted by a peripheral nerve to the centre, and then affects the part from which the stimulus is transmitted. The state of the blood, or something contained in it, may also act as a *stimulus*.

Whether the vaso-motor centre can act automatically without any extrinsic stimulus is an intricate physiological question which need not be here discussed. It is not necessary to suppose (what indeed perhaps never occurs) that the tone of the whole arterial system is simultaneously increased. If contraction be caused in a part only, blood will be held back from this part, and the pressure in the whole system raised. Conditions of this kind, together with certain consequences following upon them, are probably the most frequent cause of a temporary rise of blood-pressure. It is, however, very improbable that permanent rise of arterial blood-pressure is thus produced. Since even the shutting off of the blood from a large arterial district, as in the ligature of the main artery of a limb, has only a transitory effect on the circulation, we cannot suppose that permanent obstruction to the passage of blood through a single organ, for instance the kidney, as in cirrhotic nephritis (granular kidney), can produce a permanent rise of blood-pressure.

If the vaso-motor centres be paralyzed (inhibited), or their connection with the arteries cut off, relaxation of tone, with consequent dilatation of the vessels, takes place, and the general arterial pressure *falls*. It is probable that this effect, too, is often produced in a reflex manner by nervous disturbances conveyed from peripheral parts; but it is not quite clear under what conditions such disturbances cause reflex contraction or reflex dilatation, respectively, of the vessels. The phenomena of dilatation have been spoken of under Hyperæmia.

A serious disturbance applied directly to the vaso-motor centres causes the phenomenon called *shock*, the obvious sign of which is a loss of tone in the superficial arteries, together with a large accumulation of blood in the splanchnic vessels. Sensations of pain also lower the arterial blood-pressure, and certain drugs have the same effect, probably by causing relaxation of certain arterial territories, especially that of the splanchnic vessels.

In the above considerations we have been careful to take no account of the action of the heart. All the variations referred to would occur equally if the blood were moving uniformly, and not in an intermittent manner. Some would be very nearly the same even if the blood were at rest. We have now to consider how blood-pressure is influenced by conditions affecting the passage of blood from one part of the circulatory apparatus to another—that is, from the arteries to the veins; and, finally, the dependence of blood-pressure on the action of the heart itself.

Increase of Peripheral Resistance: Obstruction to Outflow.—The above-described variations in the size of arteries affect most all of the smaller vessels, in which the muscular coat predominates, next the medium-sized, but have little effect on the aorta. From this fact results an important relation of the contraction of smaller arteries to the heart and circulation. The contraction of these arteries, which are necessarily those most distant from the heart, hinders the outflow of blood from the arterial system into the capillaries. In other words, it increases the resistance which the heart has to overcome. There is some reason to think that the spasm of the smaller arteries may occur without the larger; but it is difficult to prove that the latter are not affected at the same time.

Thus it will be evident that if the peripheral resistance be increased, the heart's action will have to be stronger in order to produce the same uniform flow as before, with the result of increased blood-pressure. Again, since, according to well-known physiological laws, the elasticity of the arterial walls is an important factor in maintaining the circulation, rigidity or loss of elasticity increases the peripheral resistance, and so the blood-pressure.

If the arteries are relaxed, the peripheral resistance is diminished, the heart's work is lightened, and the pressure falls.

Blood-pressure as influenced by the Heart.—Having considered the influence of variations in the blood and in the capacity of the vessels on the arterial blood-pressure, we have now to consider how it is affected by the force of the heart's contractions.

The tension in the arteries obviously depends upon the force of the blood-current and the amount of resistance which it has to encounter in the arteries and capillaries. If the left ventricle contracts more forcibly without the resistance being diminished, the pressure must rise. If it contracts more feebly, the pressure will fall.

If the peripheral resistance be increased, some mechanism, not yet precisely understood, exists by which this increase is, in normal conditions, always followed by a more forcible contraction of the heart, so that the obstacle is overcome, while at the same time the pressure rises.

Causes of Increased Arterial Pressure will then be: 1. More forcible contraction of the heart, which may be produced *physiologically* by abundant food and increased vigor of the body generally; *pathologically*, by hypertrophy of the heart, unless there be some compensating defects, such as imperfection of the valves, or weakening of the muscular substance of the heart (by degeneration). Certain drugs, also, such as digitalis, etc., have a transitory effect, and iron a more permanent effect in strengthening the heart and thus raising the arterial pressure.

2. Increase of the peripheral resistance. This resistance depends upon (*a*) the state of the arteries; (*b*) the state of the capillaries.

(*a*) Resistance in the arteries is increased by temporary narrowing, by contraction of their muscular walls, especially in the smaller arteries, by rigidity, or loss of elasticity in their walls, and by any causes (such as the disease atheroma) which permanently diminish their calibre.

(*b*) Resistance in the capillaries depends on friction, and thus is influenced by variations in the calibre of the capillaries, which are, however, as yet imperfectly explained. It is also influenced by the relations between the blood and the capillary wall. If the latter be dead, necrotic or even degenerated at any part, blood passss through with more difficulty. It is not, however, known as yet that there is any general condition of this kind in the systemic capillaries as a whole. In the pulmonary circulation imperfect respiration causes an obstacle to the passage of blood through the pulmonary capillaries, with consequent rise of pressure in the pulmonary artery and right ventricle, showing the effect of altered relations between the vessels and the blood. It will follow that a change in the blood might be the cause of its finding a greater resistance in the systemic capillaries; but it is not clear what kind of change has this effect.

Increased peripheral resistance produces, generally speaking, slower action of the heart.

Causes of Lowered Arterial Pressure will be: 1. *Weakness of the heart*, which may be produced by want of food, inanition, or any form of cachexia, anæmia, etc., or by change in the muscular substance of the heart, such as fatty degeneration, or by defects in the valves which interfere with the proper expulsion of blood from the left ventricle.

Certain drugs also weaken the action of the heart, as antimony, mercury in large doses, and most metallic poisons, strong purgatives and emetics.

2. *Diminished peripheral resistance.*—Practically this refers only to resistance in the arteries, which is diminished whenever the walls are relaxed and the tone lowered in the whole or any considerable division of the arterial system. These are the same conditions as those of an increase in the volume of the arteries already pointed out, and these two effects are produced concurrently, since it is evident that a widening of the arterial channels causes less resistance to be offered to the flow of blood.

Diminished resistance will, as a general rule, accelerate the action of the heart.

Relations of Blood-pressure to Pulse.—The variations above spoken of in the mean arterial pressure have no necessary relation to the pulse. The effect of the pulse-wave in the artery is to produce a momentary rise of pressure, followed by a fall. The apparent height of the pulse-wave depends upon the difference between these two extremes, not upon the mean pressure. We may have a strong puls with a high or a low pressure, and so of a weak pulse. Hence the following combinations are possible.

Strong Pulse with High Blood-pressure.—This occurs when the peripheral resistance has been increased in consequence of some affection of the arteries, and the heart has undergone a compensatory hypertrophy. The pulse is described as "strong and hard." It is seen in many cases of Bright's disease. A similar condition is produced by ergot, which contracts the arteries.

Strong Pulse with Low Blood-pressure is found when the peripheral resistance is diminished by relaxation of the arteries without the force of the heart being impaired. It occurs in "sthenic" inflammations, in early stages of fevers. The pulse is described as "full and bounding."

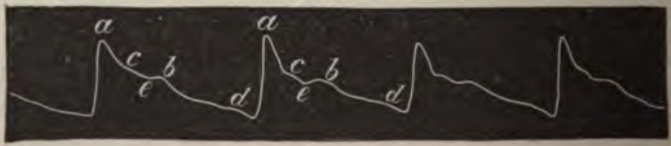
A similar condition is produced by nitrite of amyl, nitro-glycerine, etc., which produce relaxation of arteries with violent throbbing. It is generally the condition of active (paralytic) hyperæmia.

Weak Pulse with High Pressure is seen when the resistance is increased, but the heart enfeebled; so that the circulation is carried on with difficulty. It is observed in later stages of Bright's disease. A similar condition occurs in peritonitis and other abdominal inflammations, and is called the "small wiry" pulse.

Weak Pulse with Low Pressure.—This indicates weak action of the heart and want of tone in the arteries. It is found in heart weakness from any cause, as in anæmia, collapse, etc. The most marked form occurs in collapse preceding death, or in *shock* from injury. The pulse is called small and compressible.

Recognition of High and Low Arterial Pressure or Tension.—In experiments on animals these conditions are recognized by a manometer inserted into the artery, but in clinical observation they are known by the amount of external pressure necessary to compress the arteries completely. The instruments used for this purpose are not perfectly satisfactory, but some valuable indications are given by the sphygmograph.

FIG. 7.



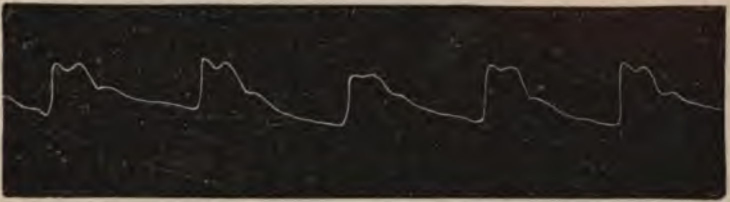
Pulse-trace from healthy man.

a = summit wave; c = tidal wave; b = dicrotic wave; e = aortic notch; d = end of line of descent, commencement of ascent.

If we take Fig. 7 as a typical pulse-trace, it shows the following features: (1) line of ascent, (2) summit wave, (3) tidal wave, (4) dicrotic wave, (5) aortic notch, (6) line of descent.

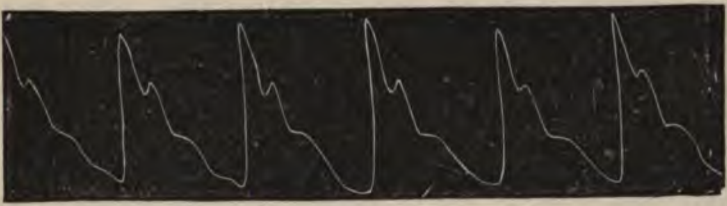
The summit wave represents the highest pressure and greatest dilatation of the artery due to the ventricular systole. After this there is a fall of pressure, but it is raised again by the first secondary or tidal wave, supposed to be due to the complete filling of the aorta and great vessels. There is then another fall, represented by what is called the "aortic notch," till another rise occurs, the "diastolic wave," due to recoil from the closed aortic valves. When this wave is excessively developed the pulse gives a double or dicrotic sensation to the finger.

FIG. 8.



Pulse-trace showing very high pressure, with feeble heart (GALABIN).

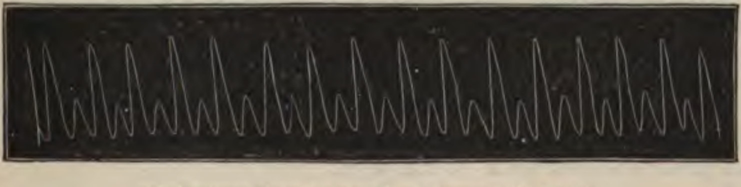
FIG. 9.



Pulse-trace showing high pressure, with very strong heart (GALABIN).

In conditions of high arterial tension the line of ascent is less lofty, the tidal wave is large and often blended with the summit wave, the aortic notch shallow, the dicrotic wave not much developed, the line of descent gradual.

FIG. 10



Pulse-trace showing very low pressure (SCHEUBE).

In conditions of low tension the line of ascent is lofty, the sum wave distinct, the tidal wave small, the aortic notch deep, the dicrotic wave well marked, and the line of descent sudden (B. Foster).

The condition of high tension is roughly recognized by the incompressibility of the radial artery, best tested by rolling the artery laterally under the finger, attending to the condition of the *wall*, not to the *pulse*. A sense of hardness and incompressibility shows high tension, unless it be due to rigidity of the walls. The latter condition will, however, generally give rise to irregular hardness, recognized by feeling the artery in a longitudinal direction.

The hardness of tension is also recognized by disappearing under the influence of nitrite of amyl, chloroform, etc., and is modified even by a warm bath.

Certain signs connected with the heart also indicate, less certainly, increased arterial tension, viz.: prolongation and sometimes reduplication of the first sound in the left ventricle, and accentuation of the second sound in the aorta, as compared with the same sound in the pulmonary artery. A strong heaving impulse, showing hypertrophy, is felt at the apex beat, different from the hurried tapping of nervous palpitation. The area of cardiac dulness is very generally increased, but not always, so that the absence of this sign must not be regarded as excluding the diagnosis of cardiac hypertrophy.

In chronic or permanent high arterial tension, hypertrophy of the heart, especially of the left ventricle, always results. There is also hypertrophy of the muscular walls throughout the arterial system. Atheroma is rarely wanting in the aorta, and is often seen in other arteries. Regarded in its most general aspect, atheroma is a thickening and strengthening of the arterial walls, caused by higher pressure and enabling them to bear it. It may be compared to thickening of the epidermis by pressure or friction. This thickening is, however, always accompanied by loss of elasticity, and thus becomes so far a hindrance to the circulation.

Increased arterial tension, as a rule, increases the amount of water which passes out in urine.

The Signs of Temporary High Arterial Tension may be thus summed up:

1. Incompressibility and evident tension of the arteries.
2. Accentuation of the second sound of the heart in the aorta.
3. Prolongation or reduplication of the first sound in the left ventricle.
4. Abundant urine, often pale and watery.
5. A peculiar pulse-trace with the sphygmograph.

The signs of *permanent* high arterial tension are the same with, in addition, some evidence of hypertrophy of the left side of the heart and perhaps of atheroma of the aorta.

Temporary rise of arterial tension is produced by muscular exertion, also, in a less transitory form, by constipation. It occurs in certain forms of headache and in *angina pectoris*.

Certain drugs, especially iron and strychnia, raise the tension.

Chronic high tension is most conspicuous in Bright's disease, especially the form called contracting granular kidney; also in general arterial disease, and possibly in a state anterior to kidney disease but leading to it.

Its most notable consequences are strain upon the circulatory apparatus, producing atheroma and other arterial changes, and, as a consequence of these, liability to rupture, that is, to hemorrhage. A certain form of headache often results.

It is a remarkable fact that anæmia—that is, the chlorotic form—is often marked by high arterial tension. This apparently paradoxical fact is probably to be explained thus: We have seen that after sudden hemorrhage there is a contraction of the arterial system, which adapts it to the diminished volume of blood and keeps up the tension. This shows that anæmia generally—*i. e.* imperfect supply of oxygen—stimulates the vaso-motor centre. Now in chlorotic anæmia, where deficiency of red globules is the main feature, there will also be deficient supply of oxygen to the vaso-motor centre, and hence it will be stimulated in the same way as by loss of blood.

Recognition of Low Arterial Pressure or Tension.—Low tension is recognized during life by the compressibility of the arteries, independently of the strength of the pulse. In extreme cases the pulse is dicrotic, producing to the finger a sensation of a double wave or a rippling pulse.

It is seen in (1) some forms of anæmia. Certain cases of chlorosis are, however, an exception, as in them the pressure may be normal or even high. The explanation of these cases has just been suggested.

2. Weakness of the heart from any cause. Hence in fatty degeneration of the heart, or in the degeneration of the heart substance which occurs in fevers. These states of the heart are accompanied by weakness of the first sound. The same result is produced by inanition, and by the action of substances which depress the cardiac force—*e. g.*, antimony.

3. Imperfect action of heart from defect in the valves, especially leakage at the mitral valve, which prevents the pressure in the left ventricle from rising to its normal amount, and thus lowers the arterial pressure generally.

In all these cases the arteries are small or comparatively empty.

4. In the condition of fever which, by vaso-motor paralysis, causes dilatation of arteries and diminishes peripheral resistance. Here the artery is full but soft, and the pulse may be large. In extreme cases the dicrotism of the pulse is well marked.

Low pressure is produced by the action of purgatives or any cause producing copious intestinal discharges, and in its extreme form passes into collapse.

Also by certain drugs, such as nitrite of amyl, nitro-glycerine, and the nitrites, which produce vaso-motor paralysis. Also by alcohol and chloroform in certain doses.

The consequences are general weakness and, if the condition be of long duration, imperfect nutrition, probably from deficient transudation of blood-plasma into the tissues.

In the condition of low pressure the urine is scanty, since the amount of urinary water, independently of the solid constituents, appears to vary directly as the pressure in the capillaries of the Malpighian tufts. When the blood-pressure in the aorta falls below forty to fifty millimetres the excretion of water by the kidneys is entirely arrested (Power's *Human Physiology*).

CHAPTER IX.

INFLAMMATION.

SINCE this is, perhaps, in its practical bearings, the most important subject in pathology, it is very necessary to have clear notions of what we mean by it.

Numerous definitions have been given of inflammation. That of Celsus was at one time familiar to all medical students, but in the present day may have to be quoted: "The marks of inflammation are four—*redness* and *swelling*, with *heat* and *pain*."

These four characters are sometimes called the cardinal signs of inflammation. Translated into modern pathological language, redness and heat are signs of arterial hyperæmia. Swelling depends upon vascular fulness and exudation, while *pain* is the result of the action of the other changes on the sensory nerves.

Now it is a matter of familiar observation that changes such as these can be produced in external parts by injuries chemical, physical or mechanical, provided the injury be not so powerful as entirely to destroy the vitality of the part.

A finger absolutely destroyed by forcible crushing, a portion of skin killed by caustic, any part of the body rendered necrotic and lifeless by frost, is not said to be inflamed, as it is manifestly incapable of the above-mentioned changes; but neighboring parts, or those which have undergone a slighter degree of the same injury, will show active hyperæmia with swelling and disturbance of sensation—*i. e.*, inflammation.

It is, therefore, clear that injuries can produce inflammation, but it is not at first sight clear whether all inflammation is the consequence of injury. In many cases, especially in internal parts, the change appears to be spontaneous.

But even these apparently spontaneous inflammations resemble those produced by injuries, and may be reproduced by injurious agents. For instance, supposed spontaneous peritonitis is precisely like the inflammation produced by a wound of the peritoneum or by the injection into it of some noxious substance. Inflammation of the pericardium may arise in the course of Bright's disease, or of rheumatism, precisely resembling the artificial inflammations excited in serous sacs by chemical irritants. It is, therefore, reasonable to conclude that in the apparently spontaneous cases some injury will be traced, if all possible sources of such are sufficiently examined.

In the case of serous inflammations occurring in Bright's disease there is a morbid state of the blood, which gradually lowers the nutrition of the body till some part or other falls into the condition which would result from a chemical irritant, or from extremes of temperature; injurious substances contained in the blood also concurring in effect. Other apparently spontaneous inflammations are attributed with probability to a primary disturbance in the nerves, which alters the nutrition of a part of the tissues, and makes it liable to injury from ordinary causes. An instance is the occurrence of bedsore in consequence of disease or injury of the spinal cord. The effect of the spinal injury in altering the nutrition of the tissues cannot be doubted, but the effects are seen in the parts which are exposed to pressure, and where the blood stagnates.

Thus many inflammations are attributable to the effects of a slight injury, combined with those of disturbed innervation, or changes in the composition and distribution of the blood.

Definition.—We may thus provisionally define inflammation as "the series of changes produced in a part by some injury, provided this be not sufficiently intense entirely to destroy the vitality of the part." Such an injury may be *mechanical*, *physical*, *chemical*, or, if the effect of living organisms, what we may call, for the want of a better term, *vital*.

But since inflammation goes on so long as the part is damaged, and ceases when the part is restored to its original condition, we may go further and say broadly that the inflamed condition is the condition of damage, or, in other words, that *inflammation is damage*. All its various phenomena may be explained as resulting from the damaged condition of different tissues or elements.

Structural Changes produced by Injury.—This conclusion involves one important postulate, namely, that the same change is produced by all injuries, and within limits this is true. That is, we only regard and apply the term "damaged" to the change common to all these causes, though there may be some other changes special to each.

The action of injuries of course varies with the tissue injured, and some tissues are more affected by some kinds of injury than others. But even allowing for this, if we take any single element or tissue we find that all the injuries, recognized as the cause of inflammation, produce an alteration in it which is substantially the same in all. This alteration may be broadly spoken of as partial necrosis or local death, and its results will be different according to the elements affected.

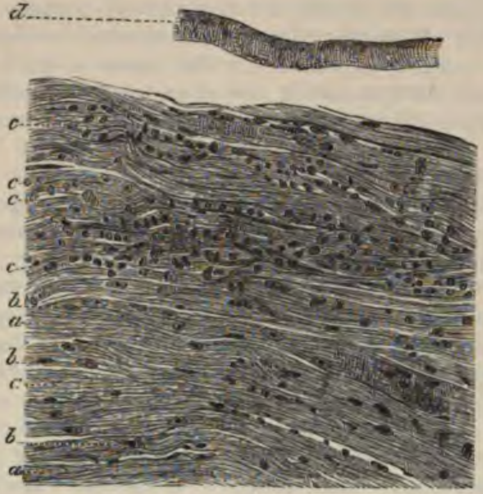
The tissue-elements of any part of the body may be most conveniently regarded as consisting of the tissue-cells (connective, muscular, epithelial, etc.), the bloodvessels and lymphatics, and the nerves.

The effect of injury on the cells is naturally the simplest phenomenon. Here we see nothing but destruction or damage in various degrees. The cells lose their translucency, become granular—*i. e.*, show, in the first place, minute granules which give a cloudy appearance, and very often become swollen, so that this change was called by Virchow cloudy swelling, or parenchymatous inflammation. This change is seen most simply in epithelial elements, which further show their loss of vitality by falling off from their attachment—*i. e.*, by desquamation or being shed. A very slight injury, of whatever kind, is sufficient to cause this.

In connective-tissue cells the changes are somewhat ambiguous. They swell up, lose their regular outline, and often appear to become converted into several elements. This breaking up or division of the cell is by some regarded as a process of growth, by others as disintegration. The subject will require further consideration. But provisionally we must state what we believe to be the ultimate conclusion: that injury by itself never produces growth directly, though it may give rise to new-formation indirectly and subsequently.

In connective-tissue fibres, again, the results of injury are somewhat obscure; but we can generally see that the fibres become somewhat swollen, looking broader than natural. But it is very difficult to regard the changes in connective tissue apart from changes in the bloodvessels. Voluntary muscle, being a very sensitive structure, shows the effects of injury very clearly. The fibres lose their striation, become more homogeneous, or, as it is said, vitreous, and, with a more intense degree of injury, become granular and even fatty (Fig. 11).

FIG. 11.



Muscular tissue from pharynx in scarlatina, showing earliest stage of injury.

a, muscle-fibres which have lost their striation; *b*, nuclei of muscle, in some cases enlarged; *c*, leucocytes of the interstitial tissue increased in number; *d*, healthy muscular fibre for comparison.

Physical Change produced by Injury.—Without going further into details we may say that the above are visible *structural* alterations which result from the action of any injury on tissue elements. But there is one general *physical* change in the tissues apart from the bloodvessels which is of great importance. They become less resistant, more distensible, and further suffer a loss of elasticity.

By elasticity is, of course, meant the power possessed by anything which is stretched to return to the bulk it had before. Injured tissues then, if distended, have lost wholly or partially the power of contracting again.

We may digress a moment to make this important point clear. Arterial hyperæmia of the skin, for instance, causes swelling, as may be seen in the ear or the face as a consequence of derangements of the sympathetic nerve. If the tissues are healthy, this swelling subsides instantly when the hyperæmia ceases, their elasticity causing them to return to their former state.

But if the tissues of the skin have been injured, as by the stroke of a whip, then the momentary hyperæmia causes swelling which is not momentary—that is, we see what is called a wheal, which is generally notably *anæmic*. Whether this swelling is due to exudation of serum or not, does not matter for our present purpose. It is, at all events, the loss of elasticity in the tissues which either permits the exudation or makes it impossible for the tissues to drive the excess of serous fluid into the lymphatics, and so restore the equilibrium.

We may then conclude that injured tissues are more distensible than normal, and also are imperfectly elastic.

Action of Injury on the Bloodvessels.—If we take the simpliest form of bloodvessels, capillaries, the cells which compose them may be seen to undergo, under the action of injuries, a change similar to those of tissue-cells; that is, they undergo granular disintegration, passing into fatty change. In larger vessels the changes are too complicated to be expressed in any simple formula, since they involve all the various tissues contained in the walls of these vessels.

But any visible structural alterations are unimportant compared with the physical results of injury to bloodvessels, which may be traced by direct observation. It is clear, from observations which will be described hereafter, that the effect of injury on vessels is, speaking broadly, like that of injury of tissues. They become less resistant, more capable of distention, and less able to recover from distention—that is, less elastic. Furthermore their walls become less capable of holding in their contents. A severe injury causes extravasation of blood; and this result follows not only on mechanical injury —*i. e.* rupture, but on the action of poisons, such as in certain cases of arsenic and phosphorus, and of powerful ferments, such as snake poison.

A lesser degree of injury causes increased transudation of the liquid portion of the blood, and of the leucocytes; as will be seen hereafter.

The results of injury of bloodvessels form the most important part of the pathology of inflammation, but must not be regarded as making up the whole of this process.

Action of Injury on Nervous Structures.—The first effect of injury in medullated nerve-fibres is seen in a breaking-up of the medullary sheath, which appears to be their most sensitive portion. The axiscylinder appears to be more resistant, at least so far as visible changes are concerned (Perls).

Ganglionic nerve-tissue is more sensitive to injury than conducting fibres. A very slight injury which leaves other parts unaffected will cause disintegration and total death of the ganglion cells.

The *functional effects* of injury on nerve-structures are also very important. With respect to the conducting nervous system it may be broadly stated that every kind of injury produces pain. This is true of pressure, heat, cold, chemical agents, etc. So universal is this law that it may be formulated in a converse sense—viz., that pain is the expression in consciousness of injury to the peripheral nervous system, provided, of course, that the part be still in connection with the seat of consciousness, the brain. The only apparent exception to this law is the fact that cold, when extreme, produces anæsthesia; but it is clear that this is due to the conducting apparatus being rendered functionally inactive by want of blood-supply; for when the blood returns, pain is felt.

Now pain is, as we have said, one of the cardinal signs of inflammation. Hence we have, in this broad and universally accepted fact of the relation of pain to nerve injury, a confirmation of the principle, that damage to the tissues is the essential fact in inflammation.

It is also a general principle that injured parts are hyperæsthetic, *i. e.*, tender, and the same is seen in inflamed parts.

Ganglionic nerve-tissue is known to be, by itself, little, if at all, sensitive, as we see in the cerebral cortex, and its functional disturbance by injury is expressed in other ways. That actual destruction of ganglion-cells must produce functional incapacity so far as it goes, need hardly be pointed out. But there is a more general principle, established by a long series of clinical observations, which is worth attention. It is this: that a slighter degree of the same injury which causes destruction of nerve-substance causes perverted functional activity, and this may have the appearance of overaction.

For instance, when the poison of fever, such as typhoid, affects the brain, its first result is to produce delirium or excitement; but a higher degree of the same injury results in coma, or perhaps death with cerebral symptoms. If the patient recover, his symptoms often show, for weeks or months afterward, that the brain has been structurally damaged. In other diseases of the nerve-centres, spasm or convulsions represent an early stage of a change the final result of which is paralysis. The same progression or succession of excessive functional activity, followed by functional incapacity, and ending in structural damage, is seen in various inflammations affecting the brain.

The further evidence that the conditions recognized as inflammation are the same as those known to be produced by injury can only be given in describing the inflammatory process.

Before going farther we must, however, touch on one important point, viz., **the relation of injury to repair.**

It is a general law of living organisms that they have a power of repairing injuries. If it were not so, they could hardly exist at all. Metaphorically this may be expressed by saying that they are in a condition of stable equilibrium, so that after a small disturbance they tend to come back to the condition in which they were before.

Hence directly an injury takes place, processes are set up which end in repair. If all the processes which arise out of the injury are considered as leading to this result, then inflammation must be regarded as essentially a conservative process, leading to the restoration of injured parts, and this is actually the light in which it is regarded by some pathologists. On the other hand, considering that repair may be accomplished with at least very little inflammation, and that the less inflammation there is, the more satisfactory is the result, others have regarded it (with Hunter) as an accident which only hinders repair, or at least prolongs the process. The results, moreover, of antiseptic surgery are taken as tending in this direction. These two views seem entirely opposed to one another, and the question which is right is an extremely difficult one.

Perhaps the points at issue may be best explained as follows: Healing without inflammation, or healing by the first intention, is only seen in perfectly "clean" wounds; for instance, in a cut with a very sharp, clean knife. Now if the divided surfaces are at once brought into apposition, the actual injury inflicted is really very slight, and the process of repair is so rapid that there is no inflammation, or hardly any. But if the surfaces are not clean, and injurious substances from outside are introduced, healing is delayed and the phenomena called inflammation are observed. In like manner it is possible that if the organism is not healthy, injurious substances may be brought to the wounded spot by the blood. In either case the inflammation is the response of the organism, not to the original wound, but to the additional injury caused by these injurious substances; and there is reason to believe that it, or at least some part of the processes included under this name, is the means by which these substances are removed or neutralized. While, then, it is perfectly clear that inflammation is a sign of protracted or hindered healing, it would seem that this hindrance or delay in the healing process is attributable to the secondary injury caused as above described, not to the means by which this secondary injury is compensated.

The aim of the surgeon, then, is not so much to prevent inflammation as to keep off, or minimize, the introduction of the injurious substances and the secondary injuries consequent on them, which, in strictness of speech, constitute inflammation.

Now, since inflammation is certainly not necessary to the healing of the primary injury in the case supposed, but appears to be the inevitable and necessary process before the secondary injuries, which depend upon the introduction of foreign substances or poisons into the wound, are compensated, some pathologists regard inflammation as a conservative process, the special use of which is to remove or expel the *noxa*—the foreign body, virus or poison. A definition of inflammation has, indeed, been framed on this basis.

According to the definition already laid down, this view is much too narrow, and accounts for a part only of the inflammatory process; but, in order to exhibit clearly what this theory does not account for, let us take another instance. Let there be a foreign body, such as a bullet or a splinter, imbedded in the muscles. In rare, though conceivable, cases this body may remain perfectly quiescent, not doing any harm or causing any annoyance. In such a case there will be no inflammation. But if it injure the tissues in any way, inflammation occurs. In other words, it produces the injury called inflammation.

But now mark the result. While the foreign body was quiescent it had no chance of being eliminated, but inflammation, especially in the form of suppuration, tends to remove it, and will probably, sooner or later, cause the expulsion of the bullet.

Hence inflammation has its conservative or sanative side, and on this ground has been regarded as a process intended to eliminate injurious substances. The real truth in the matter can only be seen on studying inflammation in detail. It will then be seen that the conception of it as an eliminative process is true of certain parts of the process, viz., of the vascular phenomena or inflammatory hyperæmia, and of exudation more especially in the form of suppuration. But it is by no means true of inflammation in the wide sense in which it is here considered.

Special Phenomena of Inflammation.—In studying the special phenomena of inflammation, it is convenient to make one broad division, viz., into (1) the phenomena observed in the bloodvessels and circulation, and (2) those observed in the tissues apart from vessels, and in non-vascular parts. It might seem more natural to speak first of the tissue changes, and of non-vascular parts; but in the higher animals the whole process is so closely connected with circulation that it is practically more convenient to begin with the processes actually observed to occur in the bloodvessels, since these may, as the others cannot so conveniently, be studied continuously in living animals.

These vascular phenomena of inflammation are studied by observing the transparent parts of cold-blooded animals, such as frogs. The web of the foot, or, still better, the mesentery or tongue, has been used for this purpose. They are spread out in such a manner as to be exposed to the air under the microscope. Inflammation may be excited by any chemical stimulus or by a slight wound; but this is not absolutely necessary, since the mere contact of air and the drying up which occurs are in most cases sufficient. The observation of warm-blooded animals is more difficult, but has been effected by special means, as regards the mesentery, for instance, in the hands of Burdon Sanderson, Stricker, Thoma, and others. Without entering into technical details, we will describe what is seen, under such circumstances, in the mesentery or tongue of the frog.

Process of Inflammation in the Bloodvessels of the Frog.—If the bloodvessels of such a part, exposed in the manner described, be carefully watched, we observe a gradual dilatation, first of the arteries, then of the veins, the capillaries being little affected in the earlier stages (immediate irritants sometimes produce a transitory contraction before the relaxation, but this is not constant). This dilatation is generally accompanied by an *acceleration* of the stream, most noticeable in the arteries. This "primary acceleration" is sometimes wanting, sometimes so short in its duration as to be hardly perceptible; and in general does not last longer than from half an hour to an hour.

So far the changes observed are identical with the condition of active hyperæmia, and if the action of the irritant were now discontinued the disturbance of circulation might pass over, and all return to the normal state.

The causes of these disturbances have already been discussed, in speaking of active hyperæmia (p. 28). The most important point is that there is an enlargement of the whole blood-stream, and that much more than the normal quantity of blood passes through the part.

Retardation.—The next change observed is one special to inflammation, namely a slowing of the blood-current in the affected area, at the same time that the dilatation goes on increasing. That is, while blood is continually being brought to the spot, and in excessive quantity, there is some obstacle to its passage through, whereas in simple hyperæmia the current is more than usually free.

The cause of this retardation has been held to be the widening of the channels through which the blood flows, by enlargement of capillaries, etc. But this explanation would only suffice if the amount of blood supplied by the arteries were supposed constant, which is not the case, since this amount is certainly increased, which constitutes the fundamental difference between pure stasis and inflammation.

Even if the supply of blood to the part were not increased, it does not appear that widening of the channels would in this case account for a slowing of the current. Where a river widens from a narrow gorge into a wide reach, the current, it is true, becomes slower. But in what are called by physicists capillary tubes, it appears that, according to Poiseuille's laws, the same rule does not hold. When liquids are flowing through such tubes, widening of the channel increases instead of diminishing the flow, apparently because the friction of the liquid against the walls is lessened. Now even the arterioles of which we are now speaking are to the physicist capillary tubes, and accordingly their dilatation will produce acceleration, not retardation; and the dilatation of arterioles in inflamed parts often amounts to a doubling of their diameter—even, it is said, sometimes more.

We have further direct evidence that the amount of blood brought by the arteries is increased, in the visible pulsation of small arterioles which before were too small to show it. Further, looking on the veins, it may often be shown that the blood in them is brighter than normal, or more arterial.

More blood is also discharged by the veins. Cohnheim found that if one forepaw of a dog was brought into the state of acute inflammation, and one of the large veins of the leg opened, the amount of blood flowing out was nearly double that flowing from a vein of the unaffected limb in the same time.

Dilatation of the blood-capillaries is generally very slight, and sometimes inappreciable, so that it is a question whether they are dilated at all, but even a small increase would involve a large addition to the amount of blood passing through.

It is, therefore, clear that a far greater amount of blood passes through the part than did before the inflammation commenced, notwithstanding the observed retardation of the current. No change in the capacity of the circulatory apparatus can explain this retardation, which must then depend upon some change in the relation between the circulating blood and the walls of the vessels.

Cause of Retardation.—This has been explained by Cohnheim as consisting in a change in the walls of the vessels, which causes greater friction; and since, as will be seen, there is reason to believe that there is a change in the physical properties of the vascular walls in inflammation, this explanation is very plausible. It has also been attributed to changes in the tissues outside the vessels, especially around the capillaries, which affect the flow of blood through them. Landerer has, by some remarkable experiments, proved that the circulation in the blood-capillaries, both under normal and abnormal conditions, is greatly influenced by the condition of the tissues surrounding them. To understand this we must consider that the capillaries, with their simple thin walls, are not able to sustain, as the larger vessels do, the whole pressure of the blood which they contain. This pressure in the capillaries is not so high as in the arteries, but still it is considerable, amounting, according to Landerer, to never less than 270 mm. water, and in softer tissues thrice that amount. That is to say, the thin capillary wall may have to bear a pressure equivalent to the weight of a column of water two feet high.

Now it is plain that this cannot be wholly borne by the capillary wall alone, and hence it must be borne in part by the *tissues* in which the capillaries are imbedded.

Landerer has further shown that the fluid contained in the tissues —*i. e.*, the lymph—always shows a certain amount of fluid tension, the precise amount of which need not here be considered.

Comparing capillaries with arteries, the wall of the former corresponds to the *intima* only of the latter, and the tissues support in the former case the tension which in the latter is borne by the middle and outer coats.

Now the tissues, like the middle coat of arteries, are elastic—that is, they receive and give back again pressure exercised upon them. Hence, as the elasticity of the arterial media is a factor in the arterial circulation, so is the elasticity of the tissues in the capillary circulation. If this property be lost or impaired, the flow of blood through the capillaries will be retarded. Now, as was before mentioned, any injury—*e. g.*, inflammation—at once impairs the elasticity of the tissues. So that, on Landerer's reasoning, the state of the tissues in inflammation will be the direct cause of the capillary retardation which is observed in the circulation through an inflamed part.

Leaving now the disturbances of circulation seen in the inflamed mesentery with the remark that the characteristic features are increased flow of blood by arteries, retarded flow in capillaries, but, notwithstanding this, greatly increased outflow on the whole, we must consider the behavior of the corpuscles in the vessels of the inflamed part.

The Blood-corpuscles in Inflammation.—It is in the veins that the most remarkable changes are seen, especially in the distribution of the corpuscles.

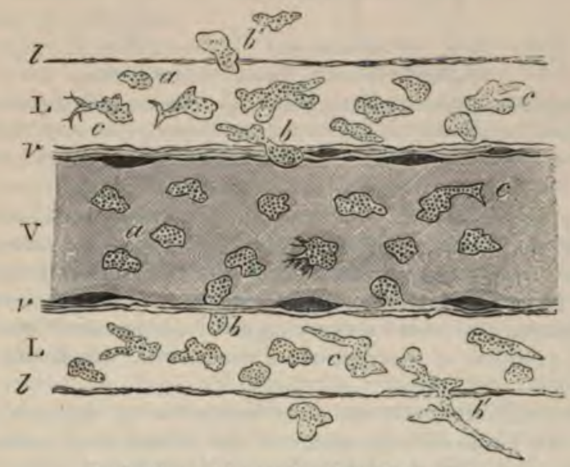
In the ordinary circulation the corpuscles of both kinds move on in the centre of the vessel, leaving a clear marginal space next the walls, occupied only by liquor sanguinis. It is owing to this that the corpuscles are never in actual contact with the vascular wall, and do not stain it. But now the corpuscles in the veins spread over the clear marginal space and touch the walls. The leucocytes, especially, drag along the walls as if adherent to them; and from time to time stand still in that position, so that a sort of layer of leucocytes lining the walls may be observed. The red corpuscles in the veins keep, for the most part, in the middle of the stream without any special change.

To these phenomena the name of *stasis* is given by most writers, and as such they were described forty years ago by W. Addison, C. J. B. Williams and others. The word stasis has, on the other hand, been restricted by some to special appearances seen in capillaries only in part of the inflamed area. These vessels become so closely filled with red corpuscles in a state of stagnation that it seems "as if the blood had suddenly coagulated within them." This is the condition spoken of before (page 36) as one of the consequences of capillary hyperæmia, and may be called *capillary stasis*. It is regarded by almost all modern writers (except von Recklinghausen and M. Foster) as a part of the inflammatory process. We follow the last-named writers in separating it from inflammation, to which a free current of blood is essential. This capillary stasis, however, is not well marked except in cold-blooded animals, and its importance in human pathology is small. It appears probable, though, that this is the condition produced in the external parts by the action of cold, a process which often leads to inflammation, but is not identical with it. We will not, therefore, use the word stasis to describe these phenomena observed in the corpuscles.

Emigration of Cells.—When the general stagnation and the *marginal position* of the leucocytes are well established, begins a process which, twice brought to light on successive occasions by two observers (W. Addison and Waller), and twice again forgotten, only secured general attention when for the third time discovered by Cohnheim.

The leucocytes, which were lying stationary on the inner side of the walls of small veins and capillaries, are suddenly observed to be, many of them, outside these vessels; and, if they be carefully watched, one can from time to time be seen in the act of passing through the muscular wall, half in and half out. First projecting as a little knob on the outer surface, it grows till it is seen as a lump of protoplasm attached by a slender peduncle, and finally, even to this last bond being separated, it appears as a free leucocyte. This process taking place at many points of the veins and capillaries, these vessels at length become covered on the outside with layers of leucocytes. In frogs, whose bloodvessels are surrounded by a distinct lymphatic space, the process occupies two stages, viz., from the vessel into the space, and from the space into the tissues (see Fig. 12).

FIG. 12.



Emigration of leucocytes (from LAVDOWSKY).

V, bloodvessel; *vv*, its walls. L, lymphatic space; *ll*, its walls. *a*, leucocytes at rest; *b*, the same passing through the vascular wall; *b'*, passing from lymphatic space into tissues; *c*, leucocytes showing amœboid changes.

In the capillaries red-blood disks also pass through the walls, usually several together at one place, so as to form a group or cluster on the outside of the vessel. This does not take place in the veins.

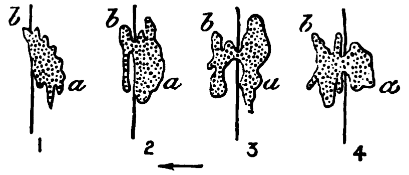
There is no passage of either class of corpuscles through the walls of the arteries.

The passage of leucocytes out of the vessels is known as emigration or diapedesis, and the same name is given with less propriety to the extrusion of the red-blood disks, which is more of a mechanical process.

The explanation of these processes is partly physical, partly vital. The distribution of the leucocytes along the walls of the vessel is probably the result of physical laws, since it is found that when a current of liquid holding fine particles in suspension is retarded, the lighter particles drag along the inner surface of the channel in which it is moving. Now leucocytes are physically lighter than the red disks.

But the adhesion of the leucocytes to the walls and their passage through are clearly the work of their vital properties, *i. e.* amœboid movements and spontaneous locomotion, as may be seen in Fig. 13, the changes of form seen being hardly consistent with anything but spontaneous movements. The process occupied from eight to thirty minutes.

FIG. 13.



Passage of leucocyte through wall of vessel.

1, 2, 3, 4 represent successive stages in the passage of a leucocyte through the wall of a capillary vessel in the rabbit; *a* = intra-vascular leucocyte; *b* = extra-vascular projection. Movement in direction of arrow. (LAVDOWSKY, Virchow's Archiv, vol. xcvii.)

Leucocytes as Carriers.—When the leucocytes have escaped from the vessels, they make their way into the spaces of the tissue (lymph-spaces), into lymphatic vessels, and, in the case of membranes, to the surface. In so doing they perform important functions in relation to the inflammatory process by carrying away foreign and injurious substances or products of destruction of tissue with which the parts are encumbered.

What special materials are thus carried away depends upon the nature of the tissue and the nature of the inflammatory process which is going on in it. In the destruction of nerve-tissue, drops of fat, or minute fatty granules, are very conspicuous; so much so that these cells, found in softening of the brain, once received a special name, that of "compound granular corpuscles." Wherever there has been extravasation of red-blood disks we find blood-pigment—rarely entire disks.

If finely divided inorganic substances, such as powdered cinnabar, are artificially introduced into the tissues, they are taken up by the leucocytes. In inflammations of the respiratory channels inhaled particles of carbon are thus taken up and may be carried away with the sputum, giving this its black color. In all these cases the relation of the transported materials to the migratory or "carrier cells" is strictly passive.

Leucocytes and Bacteria.—There are other cases in which a special importance belongs to the removal of foreign matters—namely, when these substances are microörganisms, *i. e.*, bacteria, which are injuriously present in inflamed parts. These organisms also pass into the bodies of the carrier-cells, as if the latter were attempting, as in duty bound, to seize them and carry them away. But the process is not so simple as in the case of neutral bodies. The bacterium is poisonous to the cell, and often succeeds in killing it, so that the event may be looked at from the other side as a case of an active bacterium attacking a passive cell.

But, on the other hand, the cell has the power of dealing with albuminous materials by a process known as "intracellular digestion," so that it may succeed in eating up the bacterium. There is, in fact, a battle between the intruding organism and the indigenous cell, in which sometimes one, sometimes the other, gains the victory.

Metschnikoff's Researches.—The above comparison need not be regarded as fanciful. The researches of Metschnikoff, which have attracted much attention, have established that, in certain cases, this kind of combat does take place. His observations were first made on a disease produced in a fresh water crustacean, the little "water flea," or daphnia, by a fungus.

The fungus is swallowed by the crustacean with water, and produces pointed spores, which pierce the intestinal wall and enter the tissues or the body cavity. In these parts the spore becomes at once surrounded or, so to speak, "attacked" by the blood corpuscles, which in these animals are colorless amœboid cells resembling the leucocytes of higher animals. The result of the action of the cells on the spore is that the latter swells up, becomes irregular in outline, dilates at certain spots into roundish masses of various size and irreglar form, and finally breaks up into a mass of large or small granules, pigmented and of indefinite shape, which could not be recognized as having been formed out of fungus-spores, unless the previous stages had been watched.

In the meantime the blood corpuscles become fused together into a "plasmodium," which still retains some power of amœboid movement.

It appears, then, that in this case the parasite is destroyed by the action of cells, and that this is effected by a sort of "intracellular digestion." The fusion of corpuscles into a contractile plasmodium is also very important, as illustrating the formation of "giant cells" in pathological formations, especially tubercle and allied products which are the results of the action of a specific irritant on the tissues.

Cells which perform this function of eating up living organisms, or other foreign matters are called by Metschnikoff, *phagocytes*.[1]

The converse of the story should not, however, be forgotten, namely, that innumerable leucocytes perish in the combat. Large collections of pus consist almost wholly of dead leucocytes. Hence, in a suppurating wound immense numbers of corpses, so to speak, of the elements of the body are continually thrown off. It is, I think, going too far to speak of these (with Mr. Sutton) as all killed by the action of microörganisms; for it is evident that cells in a collection of pus are placed in circumstances very unfavorable to nutrition, and moreover those extruded on a surface exposed to the air can hardly preserve their vitality long, independent of microörganisms.

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[1] For a fuller account of Metschnikoff's researches, with some confirmatory observations, see Mr. J. B. Sutton's very interesting Introduction to General Pathology, London, 1886. For the original papers see Virchow's Archiv, vols. xcvi. and xcvii.

A further confirmation of the importance of the amœboid properties of leucocytes in inflammation and repair is furnished by the observation recorded in speaking of leukæmia (Chapter XXVI.), that in this disease, where the corpuscles have lost their amœboid properties, inflammation and repair are very imperfectly performed or even impossible.

Exudation.—Along with the extravasation of corpuscles there is a considerable exudation of liquid, which, though not identical with *liquor sanguinis*, approaches it more nearly than do the fluids effused in dropsy. Inflammatory effusions generally coagulate, and in this way is formed the so-called inflammatory lymph. When the corpuscles predominate greatly, the product is called pus; the difference between this and coagulable exudation being one of degree. The composition of the various inflammatory exudations will be spoken of further on.

The explanation of the cell-migration and increased liquid exudation just described is clearly that the walls of the vessels are far more permeable than in the normal state, and more so even than in venous hyperæmia, or in dropsy. The same condition appears to retard the passage of blood inside the vessels. What change, precisely, they have undergone cannot be said with certainty; but it would appear to be the same as vessels undergo when deprived of proper nourishment.

This has been shown by Cohnheim's experiments. For instance, if blood be cut off from a portion of the vascular system, such as the tongue of a frog, by ligature of the artery, and then after a time the blood be allowed to return, no result beyond a temporary engorgement follows. But if the blood have been excluded for a longer time, (more than twenty-four hours) so that the vessels have begun to lose their vitality, the return of the blood is rapidly followed by the process of inflammation as it has been described.

The same result may be produced by the exclusion of blood from the ear of a rabbit by Esmarch's bandage, for a few minutes only, provided that the ear be at the same time exposed to a temperature of ten degrees above the normal, by immersing it in water of that temperature. On now removing the bandage and restoring the circulation, inflammation begins almost suddenly, and in an hour or two is at its height. In this case the vessels are injured by even a slight excess of heat when exposed to its influence while empty of blood.

An experiment performed by John Hunter had similar consequences. He froze one ear of a living rabbit; on thawing it the ear became inflamed, and so engorged with blood that the arteries were three or four time the size of those in the healthy ear, as shown by injection of the specimens still preserved in the College of Surgeons.

In all these cases the essential cause of inflammation was an injury to the vessels of the part, comparable to a partial loss of vitality.

It has, moreover, been shown that when the vessels of a part are in this condition, *i. e.*, inflamed, other fluids than blood are also retarded in them; for instance, milk, injected into the veins of a frog, shows the phenomena of stasis.

What is still more remarkable is that the same results can be produced in the vessels of a "salt-frog"—that is, of a living frog which has a salt-solution circulating in its vessels instead of blood.

These experiments conclusively show that the origin of the changes producing inflammation cannot be in the blood itself, but must be one affecting the bloodvessels, remembering that the vessels may be secondarily affected by the condition of the tissues outside.

Comparison of Circulatory Disturbances.—If inflammation be compared with other disturbances of circulation and transudation, we find the following differences:

Dropsy.—A change in the vascular wall permitting more copious liquid transudation. No *necessary* disturbance of circulation.

Venous Hyperæmia.—Degeneration of vascular wall from stagnation of blood leading to increased transudation and extrusion of colored corpuscles. These processes are assisted by the rise of pressure in veins and capillaries produced by obstruction.

Arterial Hyperæmia.—Increased afflux of blood causing rise of pressure in veins and capillaries; but there being no stagnation, no change in the vascular wall, such as causes exudation and diapedesis.

Inflammation.—(1) Increased afflux of blood, causing rise of pressure in veins and capillaries.

(2) Slowing of the current, owing chiefly to loss of elasticity in the tissues outside the capillaries, partly to changes in the vascular wall.

(3) Changes in the vascular wall leading to increased liquid exudation, and diapedesis of corpuscles.

CHAPTER X.

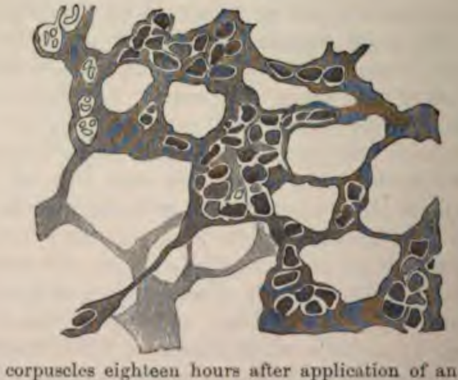
INFLAMMATION.—(*Continued.*)

Inflammatory Changes in Tissues.—The above description of inflammation is evidently a description of only that part of the process which affects the bloodvessels. It is essentially an account of the results which follow from damage of vessels, especially the veins and capillaries. But since the vessels cannot be injured without some simultaneous damage to the other tissues, we must now consider the changes which occur in the latter. These changes are important in two respects, both as regards the tissue-elements themselves, and also in so far as damage to the tissues affects the vessels and the circulation of blood in them. It now remains then to consider the changes in the surrounding tissues when the bloodvessels are passing through the processes just described; also the changes which occur in non-vascular parts.

Non-vascular Parts.—It is obvious that the changes in parts such as the cornea or cartilages, cannot be observed continuously, as in the frog's mesentery when brought under the microscope.

The results of injury are studied by touching the cornea of a frog with nitrate of silver, and cutting out the affected part within twelve or twenty-four hours afterward. In this case the only traceable changes are in the corneal corpuscles; these being, in fact, the only anatomical elements visible besides a certain number of migratory corpuscles.

FIG. 14.



Corneal corpuscles eighteen hours after application of an Irritant (HIS, Histologie der Cornea).

It is necessary to remember that by a "corneal corpuscle" is commonly understood both a protoplasmic mass with prolongations, and a space with canaliculi or branches, in which this mass and its processes are contained.

Under the influence of irritation the protoplasmic corpuscle becomes irregular in shape and the processes become shorter and thicker. Amœboid movements of the protoplasma are sometimes seen. Finally, according to some observers, the mass divides into several, which may be regarded as new cells formed by "proliferation" of the original corpuscle (Fig. 14).

But after a time it is impossible to trace any changes in the corneal corpuscles, because the spaces containing them and the canaliculi become filled with leucocytes derived from the nearest vessels, which make their way through all the anastomosing channels so that the whole tissue is infiltrated with them, and nothing else can be made out.

Since groups of leucocytes fill the spaces and occupy the place of the original corneal corpuscles, it has been thought that these groups are derived from those corpuscles in the manner above described. But it is more probable that they are migratory leucocytes derived ultimately from the blood. Cohnheim introduced coloring matter into the circulation so as to be taken up by the leucocytes; and found leucocytes which contained this matter and thus betrayed their origin, in the place of the corneal corpuscles.

If a living cartilage is injured by heat, very similar changes are seen in the cartilage-cells. These alter in shape, break up, and finally a collection of small cells is said to be found within the cartilage-capsule.

It is a question in both cases whether these small cells represent a degenerative process—that is, death of the original cells—or whether they show formation of new leucocytes or pus-corpuscles.

Changes seen in Vascular Parts.—One of the best parts for studying the effects of inflammation *post-mortem* is the peritoneum, especially the omentum. When this tissue is inflamed we find, besides leucocytes and fibrin, the result of exudation, endothelial plates, some detached, some *in situ*, which often show several nuclei, or several small cells enclosed in one. These changes cannot be regarded as actually chatacteristic of inflammation, since similar appearances are seen in the normal omentum, especially of young subjects.

In Fig. 15, drawn from the healthy omentum of an infant, we see groups of cells, which by their arrangement in groups, and by showing the effect of mutual pressure, present the appearances generally regarded as those of cell-proliferation.[1]

It seems that the changes are more active and general in an inflamed omentum, and it is also noticeable that permanent endothelial plates take on the character of young cells, showing contraction and amœboid movements.

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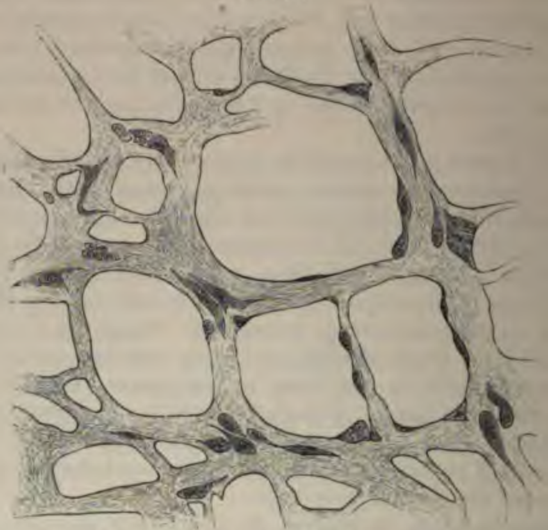
[1] This was pointed out as regards the human omentum by the present writer in 1873 (Quarterly Journal Mic. Sci., vol. xiii. p. 309), and again in the Gulstonian Lectures, 1874 (Brit. Med. Journal, 1874). Similar changes had been much more fully described in guinea-pigs, rabbits, etc., by Dr. Klein, Anatomy of the Lymphatic System, Part I. 1873.

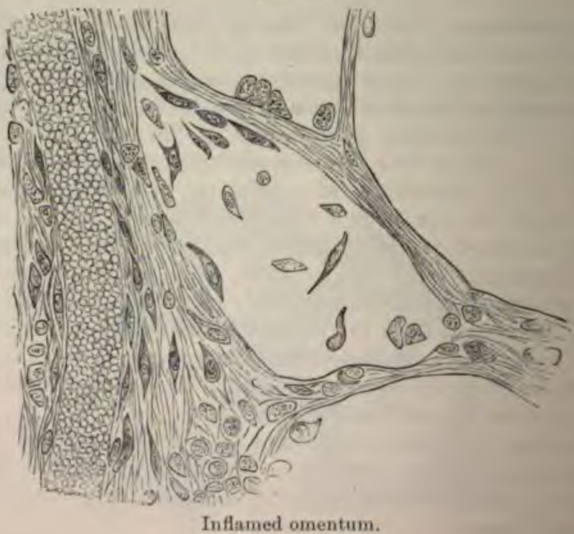
Fig. 16 represents an inflamed omentum, prepared in the same way as Fig. 15.

FIG. 15.



Cell-proliferation in normal omentum.

FIG. 16.



Inflamed omentum.

It showed a large number of leucocytes, which are here mostly omitted; but besides these there is little noticeable change in the cells; the groups of proliferating cells are hardly more numerous than normal, though some are swollen. But they are very easily detached, and hence it is difficut to estimate the original number. In fibrous connective tissue, the place of the ordinary fixed connective tissue corpuscles is often found occupied by groups of young cells, which have been thought to be derived by growth from the fixed cells, but which may also be regarded as migratory cells which have collected in the connective-tissue spaces. The appearance produced is known as small-celled infiltration.

It should not be forgotten that these tissues normally contain a small but variable number of migratory corpuscles or leucocytes, and in inflammation, whatever else happens, the number of migratory corpuscles is certainly increased.

Conclusion.—From the above observations we conclude that in inflamed tissues a large number of new, or at all events newly arrived, cells are found, which are not to be distinguished from leucocytes or migratory corpuscles. These may be found in channels of communication or occupying the place of the fixed corpuscles. Since we know that immense numbers of leucocytes do escape from the vessels, it is the most probable conclusion that these cells are derived thence. It is not impossible that some new cells are formed by changes in the fixed cells of the part, but this is not actually proved. It is also ascertained that free leucocytes may divide, that is, become converted into two; and these probably go through the same process, so that the numbers of the original emigrated cells will be greatly increased.

As an illustration, we may compare the tissue with its cells to a country with a population partly stationary and partly nomadic. Suppose that an immense immigration takes place from neighboring parts. The nomadic population will now be enormously increased, and in many cases nomads may be found occupying the abodes of the fixed inhabitants, as well as crowding all the roads and channels of communication. In such a case it would be very difficult for observers from a balloon (for instance) to say whether certain groups of individuals were immigrants or original inhabitants; and if anyone were to assert that families of the stationary population broke up their homes and joined the nomads, it would be very difficult either to prove or to disprove the assertion.

Changes in the Special Tissues of an Inflamed Part.—The remaining tissues, besides the vessels and the tissue-cells, play mainly a passive part in inflammation.

The connective tissue fibres often merely soften, liquefy, and become absorbed. In certain cases, however, a peculiar hardness is observed, which depends apparently upon thickening of the connective tissue bundles. This hardening is especially seen in those cases where a collection of pus, or *abscess*, is being formed. Hence the older pathologists set down *resistance* (renixus) as among the signs of the inflammatory swelling and as distinguishing it from simple œdema.

But the more common result is that the consistency of the tissues is diminished, muscular tissue undergoes degeneration, dies, and is absorbed or carried away.

Nervous tissue also softens and is absorbed, and the same is true of other special tissues.

The changes of epithelium are more a matter of controversy.

Epithelial cells, also, whether glandular or superficial, have been thought to produce new cells in their interior; and thus to play the same part as that attributed to the tissue-cells. But the appearances thus interpreted are explained with more probability as due to leucocytes passing into the interior of the epithelial cells. On the other hand, it is certain that a great number of epithelial cells are destroyed in the inflammation of glandular organs; and that, on mucous surfaces, the cells are shed and carried away. On the whole, the effect of inflammation on these tissues is destruction, consisting in local death. These processes are, in inflammations which end favorably, followed by repair.

Products of Inflammation.—By this term we understand substances which are exuded, or produced in the tissues as a consequence of inflammation.

Liquid exudations differ according to the tissue which is inflamed.

On serous surfaces, the inflammatory exudation differs from that of simple dropsy in containing more albumen, in having a higher specific gravity, and in being coagulable.

Exudation.	Water per 1000.	Albumen per 1000.	Fibrin.	Salts.
Pleurisy	935	55	0.4	8.6
Blister-fluid	927	50	...	8.5

Coagulability distinguishes generally inflammatory exudations from those of simple œdema in the serous cavities, but it is sometimes difficult to draw the line between slight inflammations and dropsies, as in the case of hydrocele.

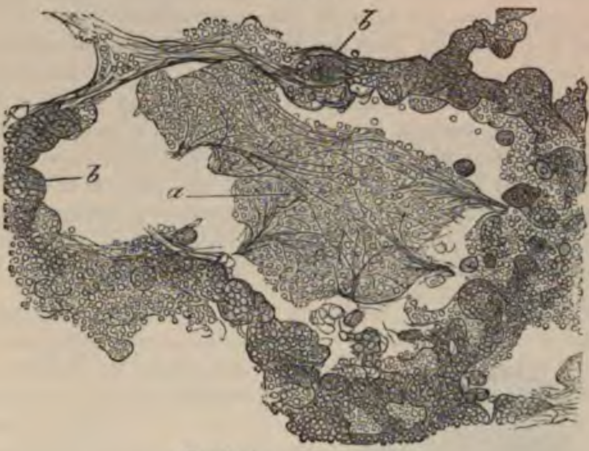
The structure of a simple coagulable exudation is well shown in the earliest stages of pneumonia, as seen in Fig. 17.

The mass, which is at first quite separable from the walls of the alveoli, consists of a fibrinous network entangling red and white blood-cells. It differs from an ordinary blood-clot chiefly in containing a few blood-disks, and a great many leucocytes, whereas in normal blood the converse is the case.

When a serous exudation contains a very large number of leucocytes it becomes purulent, or approaches to actual pus. Such exudations coagulate imperfectly. The density and firmness of the coagulum formed by inflammatory exudations is generally in proportion to the amount of fibrin present, and conversely as the amount of corpuscles. Hence the older pathologists drew a distinction between fibrinous lymph and corpuscular lymph; the former being generally evidence of a healthier state of the body.

In Fig. 18 may be seen a fibrinous and corpuscular exudation on the surface of the pleura; corpuscular exudation in the alveoli; while the fulness of the lymphatics shows that the leucocytes pass away by those channels.

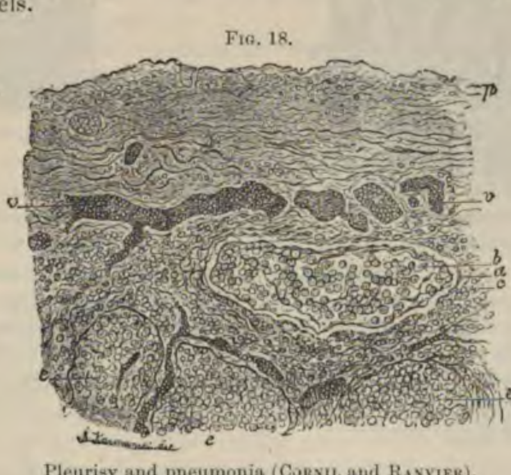
FIG. 17.



Exudation in pneumonia.

a, exudation mass, composed of fibrin, leucocytes, and a few colored blood corpuscles; *b*, capillary bloodvessels of the alveolar walls, intensely engorged.

FIG. 18.

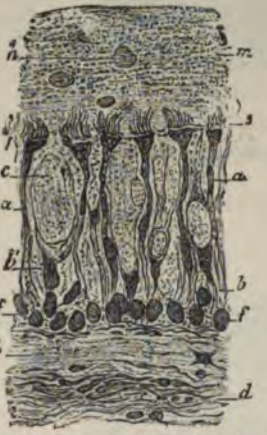


Pleurisy and pneumonia (CORNIL and RANVIER).

p, pleural surface, covered with an exudation composed of fibrin and leucocytes; *v*, engorged bloodvessels of pleura; *a*, wall of a lymphatic vessel, containing corpuscles and fibrin, *b*; *c*, alveloid of lung filled with cells (extruded leucocytes).

The exudation from inflamed mucous surfaces contains, as a rule, no fibrin, and does not coagulate. It is a little difficult to unders why this should be, since the fluid excluded from the vessels under a mucous surface must be the same as under a serous. Probably the epithelial layer acts as a filter, and intercepts some of the chemical constituents of the fluid exudation, so that on arriving at the surface it can no longer form fibrin with the constituents of the leucocytes. It has also been thought that the epithelium has some special action in preventing coagulation, like the action of the endothelium of the vessels in hindering the coagulation of circulating blood. However this may be, it is certain that when the epithelium is removed, a coagulable exudation may be formed, as is seen when mucous surfaces are acted upon by heat, blistering agents, etc., or are affected by diseases causing necrosis of epithelium. Ordinary irritants produce a mucous exudation only, but strong irritants, such as ammonia, in animals produce fibrinous exudation; and the same thing has been observed once or twice in man.

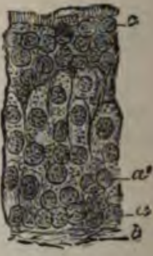
Fig. 19.



Catarrhal inflammation of trachea (Cornil and Ranvier).

d, Submucous tissue; *b*, basement membrane; *f*, *f*, round corpuscles (migratory cells) in abnormal numbers; *c*, cells in state of mucous transformation (goblet cells); *b'*, their nucleus displaced; *a*, cylindrical ciliated epithelial cells laterally compressed; *s*, cilia; *m*, free mucus on the surface; *h*, mucous corpuscles.

Fig. 20.



Catarrhal inflammation of trachea (Cornil and Ranvier).

The epithelium is infiltrated with round (migratory) corpuscles. *a a' c*. The upper layer is surmounted by cilia, which Cornil and Ranvier believe to be attached to the round corpuscles.

The ordinary exudation from inflamed mucous surfaces has much resemblance to the normal fluid which bathes such surfaces. It contains albumen and mucin, together with leucocytes (mucus-corpuscles), and a large number of epithelial cells detached from the surface.

As compared with the normal mucus, the fluid produced, for instance, in nasal catarrh appears to contain less mucin, more albumen, and more salts, especially sodium chloride. Inflammations of mucous surfaces are generally called catarrhal inflammations, or the slighter forms, catarrhs. When the number of leucocytes is very great, the mucous exudation becomes purulent, and forms a purulent catarrh.

The minute changes of epithelial cells in catarrhal inflammation are seen in Figs. 19 and 20.

The principal changes then are: (1) Increased number of cells undergoing mucous metabolism and increased production of mucus; (2) Infiltration of epithelium with migratory leucocytes; (3) Shedding off of epithelium with leucocytes.

Pus.—An inflammatory exudation, containing a very large proportion of corpuscles floating in liquid which does not coagulate, constitutes *pus*.

The specific gravity of pus is 1030–1033. It consists of a serum which is clear, slightly yellowish in tint, feebly alkaline, and coagulated by heat.

The elements suspended in it are—the pus-corpuscles, which are identical with leucocytes, albuminous granules and fatty granules.

It is difficult or impossible to separate the corpuscles wholly from the serum, and all that is known about its chemical composition refers to pus as a whole.

Pus contains water, albumen (apparently that of serum), globulin, and possibly myosin; also a large proportion of fats, viz., cholesterin, palmitin, olein, with cerebric and glycero-phosphoric acids. It is said that protagon occurs in fresh pus. The extractive matters include leucin. A substance called pyin is often found, which resembles mucin; also mucin, chondrin, and gelatin, in certain cases, according to the source of the pus.

Pus-corpuscles.—If we examine corpuscles from an inflamed surface, such as the conjunctiva, under the microscope, with a warm stage, they show the characteristic amœboid movements and changes of form, sometimes very actively. But corpuscles from a large collection of pus or abscess do not generally show this, being dead spheroidal bodies in which acetic acid develops three or more small nuclei.

Granular corpuscles—*i. e.*, leucocytes becoming disintegrated, are often seen in such cases, and molecules, both albuminous and fatty, derived from the breaking down of these bodies.

Pus left to itself undergoes at first an acid fermentation. But this is soon replaced by an alkaline fermentation in which ammonia is evolved. The latter process is set up by bacteria (bacterium termo), which, it should be remembered, are quite distinct from the micrococci which some think are the cause of suppuration in general.

The salts of pus consist of sodium chloride (in largest proportion), earthy and alkaline phosphates, carbonates, and a little iron.

The sodium chloride is chiefly contained in the serum, the phosphates in the corpuscles.

Quantitative analyses of pus differ widely. The two following are, perhaps, fair average analyses, though arranged on different principles:

	Bödeker.	Bibra.
Water	887.6	862
Albumen	43.8	91
Extractives	......	29
Pus-corpuscles and mucus	46.5	...
Cholesterin and fat	10.9	12
Sodium chloride	5.9	9
Other alkaline salts	3.2	
Earthy phosphates and iron	2.1	

Causes of Suppuration.—The liquid called pus is never formed except as the result of inflammation, but is not a constant product. It is not yet quite clear what special causes cause its production. Pus is more liable to be formed by inflammation in children, in cachectic people and possibly in those who have a special cachexia, viz., that which predisposes to tubercular or so-called "scrofulous" disease.

It is also far more frequently formed in inflammations of external than of internal parts, and the admittance of air, or of something in direct communication with air, often causes the production of pus or *suppuration.*

Hence it has been supposed that a specific poison is necessary to produce suppuration, and that this is conveyed through the air. But there is abundant evidence that suppuration may occur when the air is excluded, as, for instance, in purulent pleurisy (empyema), purulent pericarditis, etc. On the other hand it is equally clear that not the air itself, but certain things contained in the air, probably minute organisms or their germs, have a remarkable power of causing suppuration. Hence is derived the principle of *antiseptic surgery*, which consists not in excluding air, but in depriving it of germs.

When suppuration occurs in internal organs secluded from the air, it is always possible that germs may have been conveyed to the part by the blood, as will be shown in speaking of disease germs; but this is extremely difficult to prove. However, modern methods make it possible to say whether pus does or does not contain any micro-organisms; and though, as will be seen later on, such organisms are very common, there are, undoubtedly, well-marked cases of suppuration in which they cannot be found.

Heat of Inflamed Parts.—This particular feature of inflammation has always attracted very special attention, and many hypotheses have been made to explain it.

That an external part of the body is found to be hotter, when inflamed, than it is normally, or than the corresponding part on the other side of the body, is obvious.

It is also certain that internal cavities, when inflamed, become hotter than they were before. It is not proved, however, that such parts become hotter than all organs of the body. Probably some healthy internal parts are as hot as inflamed external parts; at least, there is no proof that the temperature of inflamed parts ever exceeds that of some internal parts.

If this be so, the rise of temperature is due to increased afflux of blood, and not to any production of heat within the part affected.

This is confirmed on finding that the temperature of a limb in the state of extreme active hyperæmia, such as is produced by nerve-section, may be higher than that of the corresponding limb, even when this is in the condition of acute inflammation.

This conclusion, which, though agreeing with that arrived at long ago by John Hunter, has only been established as the result of numerous conflicting statements, is of great practical importance.

It follows from this that an inflamed part does not return to the rest of the body blood hotter than that which it receives; and hence, that if the temperature of the body rises in consequence of local inflammation (as is generally the case), it cannot be merely by the return of overheated blood through the veins of the inflamed part.

There must be some other cause, which is probably the formation of some special substance in inflamed parts which passes into the blood and produces the condition called fever.

The connection of rise of the body-temperature with inflammation is further considered under the head of *Fever*.

Varieties of Inflammation.—Inflammations may be classified according to their duration; according to the part or tissue affected, according to the constitutional state or condition of the body, and so on.

Acute inflammation is that which comes on quickly, runs a rapid course, reaches an acme and then declines, like the curve of a projectile (the word "acute" meaning *rapid*, not *severe*). A common cold, acute lobar pneumonia or rheumatic pericarditis may be taken as types of this form.

Chronic inflammation may begin suddenly or rapidly like the acute form, or else may come on insidiously and gradually, but differs in this, that, instead of undergoing spontaneous decline, it will remain for a long time at a certain level of intensity, neither getting worse, nor entirely going away, like a curve approaching its asymptote. Sometimes chronic inflammation shows alternate exacerbations and remissions. It will follow that a chronic may appear to be the sequel of an acute inflammation. Instances are: chronic bronchitis or winter cough, often following an acute attack; chronic inflammation of the liver or cirrhosis, chronic gastric catarrh and the like.

It is obvious that the distinction is one of degree, and that the line is sometimes very difficult to draw.

Chronic inflammations in general show less hyperæmia, with its attendant phenomena of heat, etc.; while the exudation, cell emigration, and possibly other tissue changes, remain.

Inflammation of fibrous connective tissue (interstitial) shows very different types, according as it is acute or chronic. The former runs to abscess, the latter to fibrous overgrowth or induration. At the same time the cell changes in inflamed parts already spoken of, whatever their significance, are more noticeable in chronic than in acute inflammation.

The explanation of the difference between the acute and chronic form seems to be that in the latter the change in the vascular wall, which permits increased exudation, etc., remains, though the supply of blood to the part is not in excess. Chronic inflammation is, in fact, a condition of imperfect repair of the vessels.

Bearing on Treatment.—Without entering on therapeutic questions generally, we may point out that these differences explain the different treatment which acute and chronic inflammations respectively require.

In acute inflammation the chief object is to diminish the excessive flow of blood, so as to allow the natural processes of repair to operate, and restore a healthy condition of the vessels. Hence we use cold (as in the application of ice or evaporating lotions to inflamed parts), which contracts the vessels and diminishes the blood supply; or again, astringent metallic salts—such as those of lead, zinc, silver, mercury—in the form of solutions or ointments, and these have an effect on the vessels similar to that of cold. The same agents make the tissues more resistant and elastic—that is, they restore those properties the loss of which we have seen to be an important factor in inflammation.

Under the influence of these agents the excessive blood-flow is restrained; the vessels, no longer exposed to excessive pressure, begin to recover their normal condition; exudation and other morbid processes decline.

In chronic inflammation there is no special reason for diminishing the blood-supply, which is probably not excessive. We want to restore the nutrition of the parts, and especially of the vessels. To effect this it may even be desirable to draw more blood into the parts, which may be done by *stimulants*, *i. e.*, those agents which produce active hyperæmia—*e.g.*, aromatics. The supply of fresh healthy blood sweeping through the diseased vessels will improve their nutrition, and the exudation and other morbid processes decline. Or again, it may be useful to set up, instead of a chronic, an acute inflammation, after the cessation of which healing is more likely to occur. Or, again, we employ caustics or destructives, which sweep away the old capillaries and allow new ones to be formed which have healthier walls.

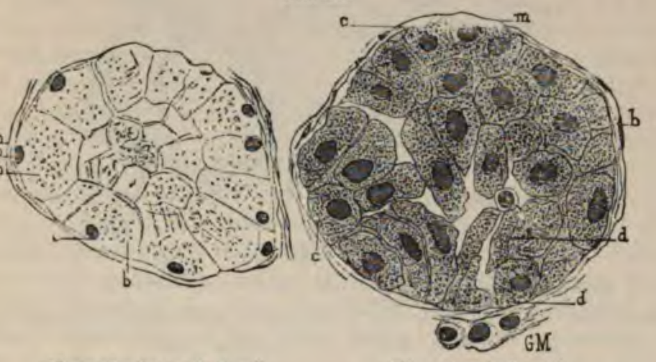
Parenchymatous and Interstitial Inflammation.—The distinction between these forms is based upon the fact that in nearly all organs it is possible to distinguish the connective-tissue framework or interstitial structure of the organ from the special elements contained in it, such as muscular fibres, nerve fibres, secreting cells (in liver and glands), and so forth, called the parenchyma. Hence, inflammation may be distinguished as *interstitial* or *parenchymatous*, according as it affects the one or the other of these constituents of the organ.

Interstitial inflammation will, accordingly, be the same in all organs, and the same as in areolar connective tissue, producing cellular infiltration in the acute form, which may lead to abscess, and induration in the chronic form.

The character of *parenchymatous* inflammation will depend on the tissue constituting the parenchyma of the organ. In the lung, inflammation affecting the air-vesicles is parenchymatous, and constitutes the different forms of pneumonia.

In the liver, kidney, and other glands changes in the glandular epithelium constitute the parenchymatous form. These changes are supposed to be analogous to those seen in inflamed mucous membranes, namely increased growth, degeneration, and death of the epithelial elements (see Fig. 21). Muscular fibres swell up and become structureless or hyaline (see Fig. 22). The only change common to all elements so situated is a granular degeneration of the cell-protoplasma accompanied by swelling. This change, also called parenchymatous or albuminous degeneration and cloudy swelling, was regarded by Virchow as parenchymatous inflammation. The name "inflammation" is not in accordance with the present usage generally given to so simple a change. Nevertheless the name is justified if inflammation be defined as damage, since these changes are the direct consequence of damage affecting the parenchymatous elements, just as the vascular and interstitial phenomena of inflammation are the consequence of damage to the vessels and the connective-tissue respectively. Formerly this change was regarded as the sign of hypertrophy or overgrowth; but, as now understood, it indicates degeneration or beginning necrosis, and only receives a special name because of its forming part of a complex process which includes, as its other parts, vascular hyperæmia and exudation.

FIG. 21.



Normal acinus of gland. The same inflamed.

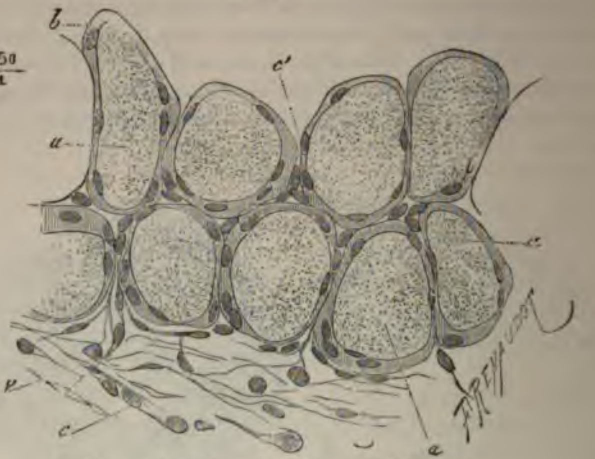
Changes of glandular epithelium in inflammation (CORNIL and RANVIER).

b, *b* (left-hand figure), clear cells containing mucus and refracting granules; *o*, nucleus.

m (right-hand figure), wall of acinus; *c*, *c*, polyhedric cells: *d*, cells flattened by compression; all swollen with granular protoplasm and large nulceus.

Certain inflammations are chiefly parenchymatous, and others chiefly interstitial; that is, they affect either the one or the other class of elements more particularly. The difference may depend upon the *nature* of the injury causing the inflammation; also upon the varying *intensity* of the injury, or upon the longer or shorter *time* during which it acts.

FIG. 22.



Inflammation of muscle (CORNIL and RANVIER).

a, granular muscle-substance; *b*, ring of protoplasm, with nuclei *c'* within the sarcolemma; *c*, inflamed connective-tissue.

These differences are well seen (as will be more fully shown afterward) in the action of poisons.

Some poisons—for instance, phosphorus—have a special power of producing parenchymatous inflammation (often called degeneration) in epithelial elements such as liver-cells or renal epithelium. On the other hand the special action of the so-called irritant poisons, *e. g.*, mineral acids or arsenic, is to produce vascular hyperæmia and interstitial inflammation. But these same poisons in a dilute or less intense form produce parenchymatous changes. An instance of the effect of the time-element in determining interstitial inflammation is seen in affections of the liver. Many poisonous agents set up acute parenchymatous inflammation of this organ, in which the hepatic cells chiefly suffer. But the poison of alcohol, though less intense, by acting continuously for a long time, sets up chronic interstitial inflammation called cirrhosis, in which the vascular connecting tissue is most conspicuously affected; though the liver-cells are at the same time very largely destroyed, either by the direct action of alcohol, or as a secondary consequence of the interstitial inflammation.

It would be a mistake to suppose that these two forms of inflammation are mutually exclusive. They are, on the contrary, generally combined, and may be regarded as concurrent effects of the same injury on different elements of the inflamed organ, a purely parenchymatous or purely interstitial process being rarely met with. The combination of the two may be seen in inflammations of the liver, such as that just mentioned, or in inflammation of muscle, as shown in Figs. 9 and 22, where, though the chief alteration is in the muscular fibres, there is commencing cellular infiltration of the connective-tissue.

In such cases the question naturally arises, What is the relation between these two forms of inflammation? Do they occur in any definite order of sequence? Are they related to one another as cause and effect? Generally speaking it seems that all elements of an inflamed part are injured simultaneously; but if there is a difference it is that the parenchymatous are earlier affected, as being more vulnerable than the connective-tissue, or even than the vessels. It may thus happen that an acute and transitory injury may severely damage the parenchymatous elements, *e. g.*, gland-cells, ganglionic nerve-cells, or nerve-fibres, without seriously affecting any other part. The circulation will, however, be secondarily disturbed by such tissue-changes, as Landerer's researches have shown. It will rarely, if ever, happen that the connective-tissue becomes inflamed sooner than the parenchymatous elements, but it is possible for the primary inflammatory change to be in the vessels, which involves interstitial exudation, and this will cause secondary changes in the other elements. Thus a large part of the degenerative and destructive changes seen in the elements of inflamed parts are really secondary, and not the direct result of primary injury. Interstitial inflammation, once established, has an undoubted effect in causing destruction of the other tissue-elements, especially, it is thought, by pressure and interference in the blood supply; but it is often difficult to prove that the interstitial inflammation is the precursor of the other changes. The distinctions drawn above have considerable clinical importance. It is only by attending to them that we can understand the differences between the several diseases which are called inflammations of certain organs—for instance, between parenchymatous and interstitial nephritis, two varieties of Bright's disease of the kidney. The same distinction may be traced in diseases of the liver, and also, though less generally recognized, in inflammation of the nerve-centres.

Relations of Inflammation and Repair.—Since, as has been said, injury in a living organism is always followed by repair, there must always be some renewal of the tissues damaged by inflammation. The peculiar feature of inflammatory repair is that, though, strictly speaking, consecutive to damage, it is always seen to be going on simultaneously with it; so that, in Sir John Simon's words, "at no stage of the process is there any show of destruction without something of renewal at its side."

The factors of inflammatory repair are partly general, partly special. The chief general factor is an increased supply of nutriment to the tissues, which in vascular parts is supplied by the exudation and emigration of leucocytes from the damaged vessels, as above described. In non-vascular tissues there is an essentially similar process, traceable in the increased flow of lymph and corpuscles through the lymphatic channels or canaliculi, as seen in the inflamed cornea;

and even here the increased supply of material must be derived ultimately from the bloodvessels of the tissues surrounding the nonvascular part.

Now since this indispensable supply of nutriment is only afforded through the damaged condition of the walls of the vessels, we see that this kind of damage is essential to the repair of the damage as a whole, and hence it is right to speak of the vascular phenomena of inflammation, viz., hyperæmia, exudation, and their results, as a salutary process tending toward recovery. If we imagine the case of all other tissues in an organ being injured, but the vessels not damaged, then the healing exudation would not be poured out, and repair would take place imperfectly or not at all. The process in such a case would be necrosis, not inflammation.

Another factor which appears to favor renewal of tissue-elements is the diminished resistance of surrounding parts. In normal conditions the elements of the body form a closely-packed mosaic, in which every cell has its growth strictly limited by the pressure of those around it. But let some of these be destroyed; those which remain are, so to speak, liberated from control, and become more capable of growth and development. With all this, we do not, however, *explain* the production of new elements, which results evidently from the independent activity of the cells.

Special reparative changes.—The special factors in inflammatory repair consist in the processes of growth by which, in the several tissues, new elements are produced. These processes are not peculiar to inflammation. In fact, they are not even pathological; for they are the means by which, in normal tissues, new elements are constantly being formed, to replace those lost in physiological waste.

Since each tissue has a mode of growth peculiar to itself, these changes cannot be brought under any general expression, and the new growth of connective-tissues alone has any universal importance in all inflammatory processes. Of the rest, different tissues vary much in their capacity for repair, sometimes being never perfectly restored if much injured.

Ganglionic nerve tissue appears to have almost no capacity for restoration; nerve-fibres and muscular fibre are restored imperfectly. Epithelium and glandular tissue recover from the effects of slight but not of very severe injuries. All special tissues have a lower capacity of repair than connective-tissue.

As instances of the special processes of repair, muscle and epithelium may be mentioned.

The repair of muscular fibre after destructive injury is seen in Fig. 22. Though the greater part of the fibre suffers degeneration, the muscle nuclei remain; they swell up and increase in number, new elongated cells are formed, the protoplasm of which becomes transversely striated, and thus elementary muscular fibres are produced.

Repair of Epithelium.—On all epithelial surfaces, including the skin, new cells are constantly being produced to replace those which are shed off. In catarrhal inflammations, the process of cell-production is more copious and rapid. It is an established law that new epithelium is always formed from preëxisting epithelium, and hence, if the layer of epithelial cells be completely removed from a certain area of the surface, it will only be restored by growth inward from the margin. New cells appear to be formed from the old by the process of cell multiplication or proliferation elsewhere described.

Glandular epithelium must be continually reproduced in normal conditions, since in many secretory processes cells are destroyed. New cells may be seen growing up side by side with the old and effete elements, but their relation to them is not always clear.

Repair and New Growth of Connective-tissue.—The repair of this tissue has a specially important relation to inflammation for the following reasons:

First, connective-tissue being present, broadly speaking, in all organs, the phenomena of its restoration are always seen in injured—that is, inflamed, parts. *Secondly*, this tissue has a greater capacity for repair than special tissues. Consequently, if the latter are imperfectly restored, as often happens, new connective tissue takes their place. *Thirdly*, the process of restoration of connective tissue often passes the bounds of mere repair, and becomes hyperplasia or overgrowth. In that case this newly formed fibrous tissue appears as if it were a *product* of inflammation, and in the sense of being a result of the inflammatory process it certainly is so.

The process of repair in connective-tissue appears to be inseparably connected with exudation and cell-emigration from the bloodvessels The first step clearly is the effusion of a coagulable exudation or inflammatory lymph. It was at one time thought that this material, called plastic lymph, was directly converted into fibrous tissue, or, as it is said organized. But more minute research has shown that the process is not quite so simple. The fibrin of the exudation appears to play only a passive part, or, at most, to serve as a sort of temporary cement. The essential change consists in the substitution for this *inorganized material* of a *true tissue*, formed out of the permanent and migratory elements (that is, out of the tissue-cells and the leucocytes) and supplied with bloodvessels which grow out of the existing vessels of the part. The "vascularization of the lymph" is an essential element of the process.

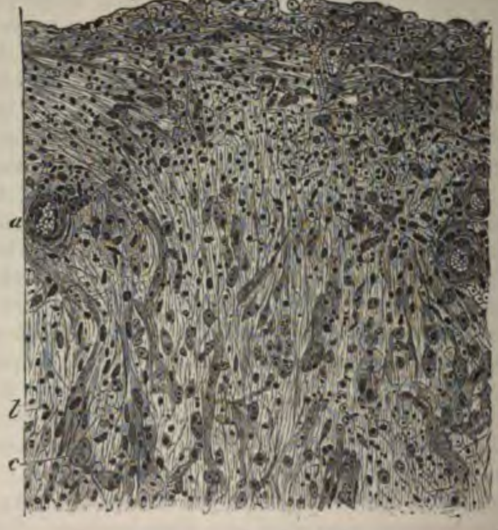
The result of these processes is the production of a sort of temporary structure which becomes converted into fibrous tissue. This temporary structure is present more or less clearly in all the so-called "plastic inflammations," that is to say, those in which new connective-tissue is formed; for instance, in adhesive pleurisy and similar inflammations of serous membranes, and in the healing of almost every kind of wound, internal and external. It also fills up the gaps formed by deep ulcers or other lesions of the skin. When it reaches the external surface, uncovered by epidermis, it takes the form of what is called granulations or "proud flesh," often projecting above the surface. Granulations supply the best type of this temporary tissue, which is hence called granulation-tissue. Though granulation-tissue is a necessary step in the process of restoration, its *persistence* is naturally and rightly regarded as a sign of imperfect repair.

Structure of Granulations.—In describing this structure we are describing what is doubtless present, in a more or less perfect form, in the internal processes alluded to above.

The general appearance of the bright red, highly vascular structure, readily bleeding when touched, and always giving off pus-cells in greater or less number, is well known. When examined in the earliest stage, a granulation appears to consist of a little mass or clump of leucocytes escaped from the neighboring vessels. There is, however, reason to think that, in some cases at least, the production of a vascular bud or outgrowth tending to form a new bloodvessel, may take place simultaneously. But Ziegler and others refer this to a later period.

We seldom see granulations in so early a stage as this. When examined later, they show the more elaborate structure represented in Fig. 23.

FIG. 23.



Structure of granulations. (300 diams.)
a, bloodvessels; *b*, leucocytes or nuclei; *c*, epithelioid cells.

Here we see bloodvessels (*a*) cut in section, but which in reality form loops, some formed fibrous tissue, and a great number of leucocytes, *b* (more numerous than shown in the figure), derived from the vessels. Besides these are other cells (*c*), which form the most important link in tissue formation, viz., the epithelioid cells, also called fibroblasts or fibro-plastic cells. It is by the metamorphosis of these that the connective-tissue fibres are formed. What is their origin? According to Ziegler (whose views are not, however, universally accepted), they are formed out of the emigrated leucocytes in the following way. While a great number of leucocytes become converted into ordinary pus-corpuscles, with multiple nuclei, and perish, others, which have but one large nucleus, increase in size, and their protoplasm becomes granular. At the same time the nucleus undergoes a remarkable change; it becomes clearer, oval, and vesicular, so as to resemble the nucleus of a sarcoma cell, the function of which is also to form fibrous tissue (*see* Chapter XXI.). The nuclei multiply by fission, probably by the indirect method called karyokinesis, and division of the protoplasm follows, so that the cells increase in number. If the cell division does not keep pace with the multiplication of nuclei, binuclear or multinuclear cells are formed. The latter, called "giant cells," are sometimes seen in granulations, but not commonly or abundantly. Cells are also said to fuse with one another, and this is perhaps one way in which giant cells are produced.

The cells thus modified put forth protoplasmic processes either at both ends, so as to form a bipolar spindle-cell, or in several directions, so as to form branched cells. The next step is the formation of connective-tissue fibres. It is a standing controversy in normal histology whether these are formed by splitting up of the protoplasm of the tissue cells, or by fibrillation of the intercellular substance. In inflammatory tissue formation, at least, it is thought that both processes occur, so that fibres originate from both these sources. At all events, the result is that fibrous tissue is formed, the nuclei of the fibroblasts remaining as the nuclei of the tissue.

The only point still remaining a matter of controversy is the origin of the fibroblasts. Those who deny Ziegler's explanation given above, believe these elements to be derived from the tissue cells of the part, which by proliferation give rise to new cells, with the characters above described, while the leucocytes undergo degeneration. The evidence that the tissue cells do give rise to new elements is very strong; and, provisionally, it may be regarded as probable that both modes of formation actually occur. Proliferation of the fixed connective-tissue cells takes place according to the method of normal parts It is remarkably well seen in chronic inflammations of the peritoneum, where figures like those of Fig. 15 are seen much more abundantly and conspicuously.

Vessels of Granulations.—The bloodvessels which form an important part of the granulation-tissue are derived entirely from outgrowths of the preëxisting vessels. According to Ziegler, this does not occur till the first fibroblasts are developed. The process of formation is described and figured in Chapter XX.

The new vessels take the form of loops or arches, and rapidly extend. They bring fresh supplies of plasma to nourish the growing tissues, and also numbers of leucocytes, some of which take part in the formative process; others are thrown out on the surface of the granulations in the form of pus-cells.

Cicatricial Tissue.—The new fibrous tissue which results from the process above described has important functions. It fills up the gaps left by the destruction of other tissues and thus forms a scar, cicatrix, or cicatricial tissue, of which the external characters are well known. It also forms inflammatory adhesions between contiguous parts, as seen, for instance, in the adhesion of opposite surfaces of the serous sacs, which often follows pericarditis, pleurisy, and similar processes. It also constitutes the so-called "fibroid tissue" which is seen in chronic interstitial inflammation of solid organs such as the liver and kidney.

In the latter cases the production of new tissue is greatly in excess of that originally existing, and constitutes a fibrous hyperplasia. It is, therefore, deleterious instead of being useful.

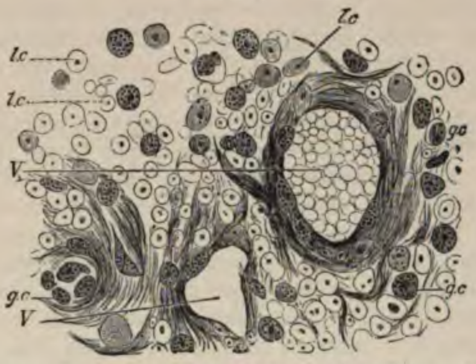
Cicatricial tissue, whether formed externally or internally, has a marked tendency, after it is once formed, to contract. Hence the notable contraction seen in superficial scars of the skin, and the diminution of bulk in organs affected with interstitial inflammation. In so doing it compresses the other tissues of the organ affected, and thus gives rise to a special form of injurious action or disease, sometimes called fibroid degeneration or fibrous substitution, but which really consists in hyperplastic production of connective-tissue, with simultaneous wasting or destruction of the other elements.

Permanent Granulation-tissue.—In what may be considered as normal or ordinary inflammations, granulation-tissue is merely a stage in the formation of fibrous tissue, and therefore essentially transitory; but, in certain specific inflammations, due to the continuous action of a specific virus, this intermediate stage toward repair (so to speak) remains permanent.

A tissue essentially the same as that above described is formed, but undergoes transformation into fibrous tissue imperfectly or not at all. Even if a fibrous scar is formed in one part, imperfect tissue remains in another and extends to neighboring healthy parts, and thus complete healing never takes place, at least until the cause of inflammation is removed. This is the case in such diseases as tubercle, syphilis, lupus. In these diseases tumors or masses of tissue are produced, which look like healing, but never heal. Hence, the analogy of these products, first pointed out by Virchow, with granulations has led to their being called granulation tumors or granulomata. And since they owe their origin to what is called an infective poison, they are called infective granulomata. The process giving rise to all these products is, however, really chronic inflammation, as will be shown in another part of this work, where the nature of the specific poisons giving rise to these diseases is discussed.

Plasma Cells.—A peculiar form of cell is often seen in granulations and granulomatous tumors, as also sometimes in normal connective-tissue, of which the functions and importance are undetermined, but which are of interest as having sometimes given rise to errors of observation. If Fig. 23 be closely examined, there will be seen, surrounding the vessels, certain cells, which are very deeply stained with the logwood dye and contain deeply colored granules. The same structures (but from a different specimen, a granulomatous tumor) are seen highly magnified in Fig. 24. These are the so-called "plasma cells" or "*Mastzellen.*" They are larger than leucocytes, sometimes much larger, of variable shape, have a granular protoplasm and a pale inconspicuous nucleus. Their most striking feature is the presence of granules, generally quite globular and sometimes remarkably uniform in size, which somewhat resemble molecules of fat, but are differently affected by coloring agents. From their being always found in the neighborhood of bloodvessels, these cells have been thought to bear some special relation to the nutrition of the tissues (hence the name ***Mastzellen*** or feeding cells), but of this there is no proof. Some observers, as Ziegler, regard them as degenerated cells, but their constant occurrence in growing parts seems to show that they are rather related to processes of growth, though in what way is undetermined.

FIG. 24.



Section of a granulomatous tumor, showing plasma cells.

V. bloodvesels; *l. c.* leucocytes; *g. c.* plasma cells (stained with methyl-violet by Gram's method). Magnified 850 diams.

Plasma cells are distinguished by their behavior with coloring matters, especially with aniline dyes. They absorb the latter with great avidity, and retain them against the action of almost all decolorizing agents. Thus methyl or gentian-violet stains the granules intensely purple and the nucleus of a paler tint, while the color is not discharged by iodine (Gram's method). In some respects their color reactions resemble those of elements in lardaceous or amyloid degeneration (Chapter XV.). When thus colored these granules have much resemblance to micrococci, and the cells containing them have sometimes been mistaken for groups of those microörganisms.

Infective Inflammations.—Besides external injury, it has been said that the commonest cause of inflammation is an infective poison, either introduced direct or conveyed by the blood. So much is this the case that some pathologists (as Hüter) have thought *all* inflammation to be caused by some such poison; others have thought that suppuration especially is thus produced. Without discussing this point fully here, it may be pointed out that many inflammations, once thought to be spontaneous, are now shown to be due to infective poisons carried by, or contained in, living organisms; and that thus the number of spontaneous or so-called idiopathic inflammations is constantly diminishing. The whole subject of infective and specific inflammations will be discussed in the second part of this work.

CHAPTER XI.

FEVER.

ONE consequence of inflammation which is always observed, if the inflamed part is sufficiently large to produce a notable effect, is the condition called fever. This condition may, however, be produced by other causes which will be spoken of presently. The essential factor in fever is a rise in the temperature of the body, but with this are generally associated certain other symptoms which may be briefly enumerated as follows: increased rapidity of the pulse and of respiration; disturbance of the nervous system shown by excitement, delirium, etc.; disturbance of the normal apparatus for regulating the temperature; disturbance of the muscular system, shown by weakness or by irregular contractions; disturbance of the digestive system, shown by the loss of appetite, nausea, etc.; alterations in the secretions of the kidneys, and probably of other glands; and, lastly, a general impairment of nutrition which leads, if continued, to emaciation and to degeneration of the various tissues. It is not clear that all these symptoms are consequences of a rise of temperature, but the latter is the only absolutely constant feature of the febrile state. The rise in the temperature of the body has, then, the first claim upon our attention, and to understand this we must first consider what are the **normal laws of temperature in the human body**.

The temperature of the body is subject to regular periodical variations, so that it is not correct to speak of any exact number of degrees as expressing the normal temperature. Makers of thermometers are in the habit of marking 98.6° F. as the normal, but this has no validity, since it only indicates a supposed average. In the case of a periodical function the average is of little importance, and in this case the determination of a true average is an almost insoluble problem. The range of temperature compatible with health in man, as measured in the axilla, is from 97.2° to 99.5° F.; in the rectum from 98.2° to 100.4°. Temperatures taken in the mouth may be regarded as intermediate between these two, there being usually a difference of about ½° between the mouth and the axilla. The temperature of children is on an average four-tenths, or half a degree, higher than in adults, and in old people it is usually somewhat lower. Temperatures below the lower limit or above the higher may be regarded as abnormal; but a temperature within these limits may, under some circumstances, be abnormal if it occur at a time when a higher or lower temperature respectively is to be expected. Variations between these limits depend partly upon individual constitution and partly upon the time of day at which the observation is taken.

The diurnal fluctuations of temperature in health are very important. My own personal observations made during several months showed that the lowest temperature occurred late at night, that there was a rise in the morning after waking, especially after getting up, and in a still more marked degree after the first meal. The maximum daily temperature often occurred in the forenoon, but sometimes in the afternoon when a substantial midday meal was taken. The general rule is that the maximum occurs late in the afternoon, and after this there is a steady fall till late at night, which is retarded, but not prevented, by an evening meal. In some persons the minimum occurs at one or two A. M.; in others it occurs about six A. M. The variations are much influenced by food, but not entirely dependent upon it, since they occur also in fasting persons. Exercise has a marked effect in raising the temperature—showing that the chemical changes associated with muscular contraction produce heat at the same time as they effect mechanical work. But since the same energy cannot appear both as heat and as work the rise of temperature is not in proportion to the work done. If a large amount of work be done in a short time the temperature may even fall instead of rise, as I have found in the rapid ascent of a height. Moreover, different kinds of exercise differ much in their effect upon temperature. External cold and heat have a great deal of effect, the body being cooled by a cold bath and heated by a hot one, but the first effect of external cold is to raise the temperature of internal organs, doubtless because it contracts the cutaneous vessels and drives the blood into internal parts. In hot countries the body temperature is, on the average, somewhat higher than in cold countries. It appears clear, however, that the body possesses the power of spontaneously regulating the temperature, since this remains nearly constant through all external changes.

This regulative power chiefly resides in a mechanism by which more or less blood is sent to the skin through relaxation or contraction of its bloodvessels. The greater the amount of blood sent through the skin the more rapidly does the body cool. If the skin be comparatively bloodless, cooling is checked and the heat accumulates in the internal parts. The cooling of the skin is effected partly by mere radiation, partly by the evaporation of water excreted by the sweat-glands. But since the amount of sweat excreted depends upon the amount of blood sent to the skin, these two factors act in normal conditions concurrently, and need not be opposed. This machinery appears to be under the control of a nerve-centre situated in the *medulla oblongata*, and acts by means of the *vaso-motor* nerves. Rise of body-temperature in normal conditions causes a flow of blood to the skin and consequent cooling. Lowering of temperature, on the other hand, withdraws blood from the skin, so that the radiation of heat from the surface of the body is reduced to a minimum.

The cooling process doubtless consists chiefly in lowering the temperature of the blood contained in the skin; the blood thus cooled being returned to the body by the veins, and producing its effects on the whole circulation. This arrangement is really facilitated by what might seem to hinder it, namely, the introduction of a bad conductor of heat, adipose tissue, between the skin and the internal organs. This makes it possible for the skin to have a temperature of its own, different from that of the internal parts. Transference of heat from the inside to the outside accordingly takes place by the circulating blood and not by direct conduction. Cooling is thus effected more rapidly than it would be in the case of a dead body or other mass of solid matter without internal movements.

Cases in which external temperature is higher than that of the body are not important for the present purpose; but it may be noted that radiant heat acting on the surface of the body reaches the internal parts in the same way; heating the blood of the skin, which passes inward by the veins.

Another means by which the blood is cooled is by evaporation and radiation from the internal surface of the lungs; and since, when the body-temperature rises, respiration is quickened, this also is a regulatory mechanism tending to keep the temperature normal. Excretion from glands causes a constant though, except in cases of sweat-glands, not an important loss of heat. It is estimated that 80 per cent. of the heat is lost through the skin; and less than 20 per cent. through the lungs.

Equilibrium of Temperature.—The temperature of the body thus, at any moment, depends upon a balance between the heat which is constantly being produced by chemical processes within the body, and the amount of external radiation and evaporation regulated chiefly in the manner just described. These regulative processes, it should be remembered, act, in health, automatically, that is to say, any rise or fall in the body-temperature at once sets in motion a mechanism by which the disturbance is compensated.

Rise of temperature may then be a consequence of increased production or of diminished loss of heat. Increased heat-production will not always be accompanied by rise of temperature; for it may be compensated by increased activity of the cooling process. Or, again, the rise of temperature may be deferred, and thus appear at a time when the production of heat is apparently not in excess.

Variations in Production of Heat.—The production of heat in the body being the result of chemical changes in food-substances or tissues, is most abundant where these changes are most active, and especially in the voluntary muscles and the glands. The muscles play the more important part, on account of their large mass, making up nearly one-half the body, and because oxidation is most active in them. The liver has a higher temperature than any other organ—104° F. (Cl. Bernard)—and the blood in the hepatic vein has nearly the same, being almost two degrees hotter than that in the aorta. In all active glands and muscles, the issuing venous blood is hotter than the entering arterial blood. Hence increased functional activity of these organs, as in muscular exercise or in assimilation of food will account for increased production of heat, which may be considered as a sort of additional or supplementary function of these organs. In normal conditions this, the so-called "thermogenic" function, keeps step with the proper function of contraction or secretion; and though we are not able to say positively that the two functions act in proportion to one another, at all events they cannot be separated. But in abnormal conditions the thermogenic function (of muscle, for instance) may be displayed without its contractile function being exercised, and by pathological experiments it has been found possible to isolate, to a certain extent, the thermogenic function. Thus Dr. D. Macalister found that stimulation of the sciatic nerve of a frog causes tetanic contraction of the thigh muscles, and at the same time a rise of temperature in them. But if the stimulation be continued too long, the thermogenic power of the muscle is lost, and there is no rise of temperature, though the power of contraction remains. Thus the thermogenic function is exhausted sooner than the motor function. This result may be compared with the personal observation quoted above, of fall of body temperature in ascending a height. It has also been found that external cold impairs the thermogenic function; and that the poison curare abolishes this; at the same time as it does the motor function of muscle; so that a curarized animal cannot maintain its temperature.

Theory of a Heat-centre.—To explain these facts it has been further supposed that the thermogenic function is under the control of a special nervous mechanism, including a nerve-centre in the cerebrum, and fibres either special or identical with motor fibres, going to the muscles. This is a difficult point in physiology which will be discussed later on. But it must never be forgotten that heat cannot be made out of nothing, and can only result from the conversion into it of some other form of physical force, or of chemical affinities.

Temperature in the Febrile State.—Now in febrile temperatures we have two conspicuously abnormal conditions: first, the temperature is actually higher than in health; second, the regulative mechanism acts in an abnormal manner. The temperature in fever may in rare cases rise to 108°, 110°, or possibly even higher; but, speaking generally, 104° or 105° indicates fever of some intensity. Wunderlich gives the following scale:

Subfebrile temperature . . .	99.5° to 100.4°
Slight fever	100.4° to 101.3°
Moderate fever	101.3° to 102.2° morning, and evening 103.1°
Considerable fever. . . .	103.1° morning to 104.9° evening.
High fever	Temperatures above these.

The commencement of fever, if rapid, is often indicated by a sensation of cold or chill, accompanied by contraction of the skin and irregular muscular movements called shivers, or rigors. But while cold is felt the temperature of the body is rising. This is, of itself, enough to show that the regulating machinery is disturbed, for it is clear that the condition of the skin hinders cooling, and, so far as it goes, tends to heighten, instead of to abate, the fever. The chill is generally succeeded by a feeling of warmth and flushing of the skin, during which the temperature may either fall or go on rising. Another abnormal condition in the heat-regulation machinery in cases of fever is the variable amount of perspiration. Very generally the increased heat of the body does not call forth the normal production of sweat, hence a hot, dry skin has always been regarded as the criterion of fever. Then again we may have copious production of sweat, by which the temperature is, at least for a time, depressed. Now, since rise of temperature can only be produced by increased production of heat, or by diminished loss of it, the question arises whether one or both of these factors are concerned in the production of fever. It has been thought that the matter could be explained by supposing that fever patients give off less heat than normal persons, and that this diminution might be enough to explain the rise of temperature. But it has been clearly proved that in the febrile state more, instead of less, heat is given off from the surface of the body, and that this increased loss may amount to one and a half times, or twice the normal. These data were arrived at by Liebermeister and others by placing fever-patients in baths and measuring the amount of heat communicated to the water. The result was that at a body-temperature of 104° or over, the patient gave off about twice as much heat in the same time as at a normal temperature. In another experiment a febrile patient placed in a bath at 8° C. lower than his own temperature gave off 36 calorimetric units at the onset of the febrile process, 56 units at the acme, and 37.5 units during the decline (a calorimetric unit means the amount of heat necessary to raise one kilogram water through 1° C.) In these instances the relative, not the absolute, quantities, are important.

Experiments made in artificial fever produced in animals, on the whole, confirm these conclusions. Dr. H. C. Wood thus sums up the result of his elaborate researches. In the pyæmic fever of dogs the heat-production is usually in excess of the heat-production of fasting-days, but less than that which can be produced by high feeding. Usually the production of animal heat rises in the febrile state with the temperature and with the stage of the fever, but sometimes the heat-production becomes very excessive, though the temperature of the body remains near the normal limit. In rabbits with pyæmic fever heat-production seems to be even greater than it is in health when food is taken.

Zymotic Theory of Fever.—It is, therefore, quite certain that in fever there must be an increased production of heat within the body, but at present opinions differ widely as to the cause of this increased heat-production. The most generally accepted view is that it is due to the presence of some so-called pyrogenic substance in the blood, either derived from an inflamed part or formed by the introduction into the body of some specific poison. Many attempts have been made to find and isolate such a body.

It has been found that pus, and other matters derived from inflamed parts, when injected into the veins, cause a rise of temperature. But the same result is produced by septic matter, and even by injecting large quantities of water into the veins of animals. It is, therefore, difficult to point to any one material as the one pyrogenic substance, though the action of pus is the most definite and constant. No one substance has yet been isolated from inflammatory matters which produces the pyrogenic effect. In all the above cases, death and decomposition of cells, either of the blood or of the tissues, occur, so that the pyrogenic substance is supposed to act like a ferment and break up the proteid matters of the tissues, causing increased oxidation. The chemical changes thus set up, both those which are of the nature of oxidation and those which consist in splitting up complex molecules into simpler ones, are undoubtedly causes of heat-production. Now we find, as a matter of fact, evidence of greatly accelerated combustion and other chemical changes during the febrile process: the amount of carbonic acid and urea excreted being both increased, sometimes to double the normal amount.

Increased Production of Carbonic Acid.—The most exact results were obtained by Liebermeister, by enclosing patients during a fit of ague in Pettenkofer's respiratory chamber, where they could breathe freely, and where the products of respiration could be measured. A patient whose weight was 62 kilos gave off the following weights of CO_2 in grammes during four periods of two hours each, febrile and non-febrile states being taken alternately:

Febrile.	Non-febrile.	Febrile (sweating).	Non-febrile.
77.6	58.1	73.5	63.9

The two febrile periods give an hourly average of 37.7 grammes CO_2, the two non-febrile 30.5 grammes. The hourly amounts given off by a healthy man under the same conditions were (reduced to the same body-weight) 28 grammes, in round numbers, while lying still, 22 grammes while asleep, and 37.5 while exerting his voice in singing and thus increasing respiration. The results agree sufficiently to show the great excess of CO_2 produced in the febrile state.

Another set of determinations was made by Regnard, by means of a respiratory apparatus applied to the mouth and nose, in which the oxygen consumed was also determined, also in a patient with ague, in two hourly periods.

	Temp.	Oxygen.	CO_2	Ratio : CO_2.
Non-febrile	99.8° F.	30·8	22.7	0.73
Febrile	104.9	63.7	42.3	0.66

These results show an important fact, namely, that the consumption of oxygen is increased in fever, in a higher proportion than the excretion of CO_2. This disproportion shows that a certain surplus of oxygen is used in the combustion of other elements of the body than carbon, and remains in the form of water or other oxidized products, not being exhaled as CO_2. This accords with the result of experience, that there is an accelerated combustion or waste of the tissues in fevers.

The above results, obtained in the acute febrile process of ague, were independent of variations in amount of exercise, amount of food taken, and so forth. In continued fevers the amount of food taken is much less than in health; and this diminishes *pro tanto* the amount of CO_2 excreted. But even with diminished diet, a fever patient may excrete more CO_2 than a healthy person, and very much more than the healthy person would on a fever diet. The increase of CO_2 as determined in a number of febrile complaints, has been found to be often fifty per cent., sometimes more.

These results have, on the whole, been confirmed by experiments on animals, in which fever was artificially excited by injecting pus or septic matters into the blood. An increase of CO_2 amounting to sixteen or twenty per cent., sometimes fifty or seventy per cent. in a fasting condition, has been observed, but the difference when the animals were well fed was much less.

Increased Production of Urea.—This increase is generally well marked in fever, if sufficient food be taken. But as fever patients mostly take very little food, there may be a loss from this cause, which the increase due to the fever may not be enough to counterbalance. The best comparison is, therefore, made in cases where the ingestion of food is not interfered with, as in the daily fever of quotidian ague. Dr. Ringer's careful observations in a case of this kind showed greatly increased excretion of urea during the ague fit, as the following determinations of urea and chloride of sodium excreted at different hours of the day will show. The patient had a rigor at 8 A.M.; the hot stage came on at 9.15, and sweating at 11 A.M. The results were the same when the patient fasted. The table shows urea produced in one hour.

Hour . .	7	8	9	10 30	12	1.15	3
Temperature . .	97.5°	98.6°	103°	104°	101°	99°	98.6°
Urea	0.65	1.47	3.47	0.64	0.44	0.10	1.22
NaCl	0.2	0.12	0.67	0.07	0.02	0.04	0.04

It will be seen that the increase of urea began with the rigor before the temperature was actually raised.

The amount of chloride of sodium was here increased proportionally to the urea, but this is only the case in ague. In most febrile conditions, on the contrary, the amount of this salt excreted is decidedly diminished. But this may depend upon other processes going on in the body which cannot now be spoken of.

On the whole, then, the increased excretion of the chief products of combustion and tissue-change, carbonic acid and urea, supply indisputable evidence of accelerated chemical changes in the body. These processes might affect the food or the tissues, but, considering the diminished supply of food, the chief weight must be laid upon the increased waste of tissues.

Summary of Chemical Explanation of Fever.—We may then take it as established that the heat of fever results from chemical processes certainly affecting the tissues, and possibly also incompletely assimilated food-substances in the body; that this change takes place partly, perhaps, in the blood, but chiefly in the tissues, and among these more especially in certain tissues, the glands in part, but most of all in the muscles. On what we have called the zymotic theory these changes are set up, or, at least, very greatly increased in intensity, by substances which have the property of breaking up the more complex compounds into others which are more readily oxidized. Such substances are called pyrogenic.

This theory is especially applicable to two kinds of pyrexia: first to that induced by the specific poisons which cause specific fevers, such as scarlatina, smallpox or malaria; and, secondly, to that induced by local inflammations and wounds. In the latter case not the injury itself, but morbid processes arising in the wounds, chiefly tend to produce fever. These two forms may be called *infective* and *traumatic pyrexia* respectively.

It is supposed that in traumatic processes pyrogenic substances are formed at the seat of inflammation or injury, which are absorbed into the blood, and circulated through the body, just as the poisons, for instance, of scarlet fever and typhoid circulate; and that in both cases heat-producing chemical changes are set up, the result of which is fever.

It is not probable that this explanation will ever be entirely invalidated. Nevertheless, there are certain objections to it. In the first place, it is urged that the amount of fever is not proportional to the amount of local inflammation. In some cases the inflammation of small parts, for instance of the tonsils, produces higher fever than that of much larger organs. In other cases a small collection of pus if shut in, as in the case of a whitlow, for instance, produces more fever than copious suppuration in less confined situations. Moreover, what is still more conclusive, there are cases of fever, or at least of high temperature, where the amount of inflammation is practically *nil*, and where there is no reason to suppose any specific poison to be concerned. It would appear then that the zymotic theory, though it may be adequate in some cases, is not of universal application, and there is room for another hypothesis.

Other Theories of Fever.—On another view the production of fever is referred to the nervous system. It is known that injuries to the spinal marrow sometimes result in an extraordinary rise in the temperature of the body—as is supposed, through a disturbance of the normal heat-regulating centres. The highest temperature yet recorded, 120°, was observed by Teale in a case of fractured vertebræ, which ended in recovery. It is accordingly supposed that the pyrogenic substance acts directly upon the nerve-centres and secondarily upon the tissues—not immediately upon the latter; but since the nervous system can only produce heat by setting up chemical changes in the body, even in that case the heat of fever is certainly due, for the most part, to chemical change, whether produced directly or indirectly. The only other conceivable source is that there may be a molecular change (not a decomposition) in some tissues, such as muscle, which is accompanied by liberation of heat. We have instances of physical changes producing heat in the rise of temperature which accompanies the passage from the viscous to the crystalline state, for example, in such substances as sulphur and sugar. But any such explanation applied to living tissues is entirely theoretical.

Nervous Theory of Fever.—The intricate question of the influence of the nervous system on fever can only be understood by considering both the physiological evidence for the control exercised by the central nervous system on the production of heat, and the pathological evidence for the effect of nerve-lesions in producing rise or fall of body-temperature.

The physiological theory, now generally though not universally accepted, may be stated as follows.

Thermogenesis or heat-production in the body is, even in health, chiefly due to chemical changes in the voluntary muscles, and this is still more predominantly the case in fever.

The thermogenic or heat-forming function of muscle, already spoken of, is supposed to be under the control of a nerve-centre or centres situated in the brain. From this centre the muscles receive fibres, which follow the same, or nearly the same, path as the motor fibres, the function of which is to regulate the production of heat in the muscular substance. This regulation is generally supposed to be effected by an *inhibitory* action of the nerve centre. This is, the fibres proceeding from it check the chemical processes in muscle by which heat is produced, and when they are *divided* or *injured* these processes go on unchecked, with the result of greatly increased heat-production. Some physiologists have thought that the influence of the heat-centre may be exerted through the vaso-motor mechanism, by influencing the supply of blood to the muscles, and thus causing a greater or less degree of chemical change. But this explanation has been refuted by experiments which show that the variations in production of heat are not directly dependent on blood-supply.

It would also follow from what has been said, that *stimulation* of the heat-centre would produce the converse effect of checking the heat-production in muscle, giving the mechanism for dissipation of heat free play, and thus lowering the temperature of the body, or of the part specially affected. There are some results pointing in this direction, but the very delicate experiments necessary to establish this point have not yet been carried out with complete success.

Aronsohn and Sachs seem to have established the existence of an actively stimulating, not inhibitory, heat-centre, by *stimulation* of which the heat production in muscle is increased. Dr. Macalister also supposes the existence of fibres, such as might come from such a centre, which have a direct effect in increasing heat-production, as opposed to the inhibitory fibres already referred to. The former he calls *catabolic*, as tending to pull down or destroy the muscle substance; the latter *anabolic*, as tending to build it up again. These intrica physiological points it will be enough to mention without discussi only laying stress on what appears to be the definite result of experiment, namely, that the production of heat in muscles is controlled, whether in the way of stimulation or inhibition, by one or more cerebral centres. It is thought by some that there may be secondary heat-centres in the cord also, but this is uncertain.

The precise locality of the "heat-centre" or centres is not definitely established. Dr. H. C. Wood has referred an inhibitory heat-centre in dogs to a limited area of the cerebral cortex immediately behind the fissure of Rolando, that is in a part of the motor area connected with the limbs, as defined by Hitzig and Ferrier. Dr. Ott states that there is in rabbits a heat-centre at the anterior inner end of the optic thalami, by stimulation of which increase of temperature results, amounting in one experiment to 7° F. in an hour. Aronsohn and Sachs place their heart-centre—determined in rabbits, dogs, and guinea-pigs, on the inner side of the corpus striatum—near the nodus cursorius of Nothnagel. They also found that, as in ordinary fever, the consumption of oxygen and excretion of carbonic acid corresponded to the rise of temperature produced by stimulation of this centre.

The one essential point is, that all agree in placing the chief heat-centre above the medulla oblongata, and, indeed, above the pons. The localization is of fundamental importance, since it excludes any implication of the chief vaso-motor centre situated in the upper part of the medulla. This latter centre has no effect on heat-production, though it does influence the temperature of the body, by controlling the dissipation or loss of heat from the surface. If this centre, or fibres proceeding from it, be injured, the tone of the cutaneous vessels is lowered, blood accumulates in the skin, and cooling proceeds with great rapidity.

For instance, if the medulla, or the spinal cord at any point above the origin of the splanchnic nerves, be divided, the temperature of animals experimented upon falls rapidly, it may be to such an extent that death results. But if cooling be prevented by enclosing the body in non-conducting materials, the loss of heat is checked, and the temperature may even rise instead of falling. These results are evidently complicated by the fact that in such experiments the thermogenic fibres proceeding from the higher heat-centres must also be divided, and this lesion, so far as it goes, tends to raise the temperature. But the fact remains that the vaso-motor mechanism influences the rate of cooling or dissipation of heat, not its production. When this is interfered with, the body in respect of its heat-regulation lies, so to speak, at the mercy of external circumstances, having its temperature largely determined by the temperature or conducting power of the bodies with which it is in contact.

But how, it may be asked, can the effects of increased production of heat be distinguished from those of diminished loss? The answer is, by calorimetry as distinguished from thermometry. Calorimetry consists in determining the actual amount of heat given off from the body, as shown by the heating effect of water or other medium surrounding it. Such experiments cannot, for obvious reasons, be made available for measuring the production of heat in the human body, but in the case of smaller animals methods too elaborate to be described here enable the experimenter to determine accurately the amount of heat given off, and thus to draw a clear distinction between the two causes of temperature-fluctuation above indicated.

Summary of Physiological Results.—The teaching of physiology respecting the influence of the nervous system on temperature may be broadly stated as follows. Heat-production in the body is to a large extent a function of muscular tissue, and is regulated by a centre, or centres, situated in the brain, injury (or it may be stimulation) of which causes increased thermogenesis or heat-production, and, as may be inferred, interference in the opposite sense causes diminished thermogenesis.

Dissipation or loss of heat is mainly a function of the skin and its bloodvessels, and is controlled by the vaso-motor centre in the medulla oblongata, injury or destruction of which accelerates cooling, and makes the temperature of the body largely dependent on external influences. Regulation of the heat of the body, or thermotaxis, is chiefly effected in normal conditions by the vaso-motor mechanism; but it is probable that the thermogenic centres have also a *regulative* function as well as a *productive* one, as complex injuries, affecting fibres proceeding from both these centres, will produce mixed or complicated results.

The temperature of the body is not a direct measure of the production of heat, but depends upon the momentary balance between gain and loss of heat.[1]

Pyrexia from Injury to Nervous System.—We must now consider the pathological evidence that lesions of the nervous system have an effect on the production of heat, and on the temperature of the body. Many instances of this have been collected by Dr. Hale White,[2] and others are recorded elsewhere. It must be understood that in no case is nerve-injury assumed to be the cause of fever, if any other cause, such as local inflammation or specific disease, was present which might have accounted for it.

Lesions of the Brain.—A rise of temperature without inflammation has been observed in the following cases:

Tumors affecting the pons Varolii or its neighborhood. A tumor pressing into the right optic thalamus and crus cerebri produced a temperature of 107°.

Hemorrhage into the pons has frequently, or indeed generally, produced great rise of temperature, even up to 110°. The same condition affecting the corpus striatum or other great ganglia, or in the centre of the hemisphere above them, has produced similar results. But the results of hemorrhage are often complicated by the phenomena of "shock."

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[1] This subject is further developed in Dr. Donald Macalister's able Gulstonian Lectures for 1887, reported in Lancet and British Medical Review.

[2] Guy's Hospital Reports, vol. xlii.

Embolism affecting the pons or the corpus striatum has produced like symptoms; and so have other degenerative changes affecting the same parts. Insular sclerosis—that is, sclerosis of limited patches of brain—is known to cause pyrexia, probably from affecting the same parts.

Now in all these cases we have a severance of nerve-fibres passing from centres above the medulla oblongata; that is precisely the change which experimental physiology would lead us to regard as cutting off communication between the inhibitory heat-centre and the muscles.

There is, moreover, in these cases no evidence of any injury to the vaso-motor centre.

It must, however, be stated that there are cases of brain-lesion in which the temperature *falls* instead of rising; or in which a fall has succeeded to a rise, or *vice versâ*. In cases of tumor this is rare, and perhaps only happens when the cord also is affected. In extreme cerebral hemorrhage, on the other hand, fall of temperature is often observed, and sometimes an extreme fall, even as low as 87.8 F. (Erb).

This phenomena has been, without any dispute, ascribed to "shock," such as is seen in severe injuries to other parts besides the brain.

By "shock" is meant a condition of which the most conspicuous feature is a loss of tone through the whole arterial system; that is precisely the condition which, as we have seen, physiology teaches to be the cause of excessive dissipation of heat, or rapid cooling. In the cases referred to we must therefore suppose that the loss of heat due to shock more than counterbalances any gain of heat due to injury of the heat-centre or its efferent fibres. Ill-defined degenerative changes in the brain are also sometimes accompanied by fall of temperature, of which the explanation may be the same. But even these facts are evidence, in any case, of the calorific mechanism being interfered with by injuries to the brain, though in a converse sense to those formerly spoken of. It should be stated that after the fall of temperature caused by shock, however produced, there is, very generally, reaction causing a rise, and this rise may possibly be independent of any other lesion of the nervous system.

Lesions of the Medulla Oblongata and Cord.—The physiological data given above would lead us to expect a twofold result of lesion of these parts, according as either the calorific fibres coming from the higher centre, or the vaso-motor mechanism, should be disturbed, and clincal observation confirms this.

Lesions of the medulla oblongata have not been clearly isolated in relation to these laws; but many instances of lesion of the cervical portion of the cord are recorded.

Tumors of the cervical cord, in which the chief effect would probably be mechanical pressure on the conductive fibres, generally produce a rise of temperature.

Injuries to the cord, commonly from fracture of vertebræ, produce sometimes a rise, sometimes a fall, of temperature.

Many cases of remarkable *rise* of temperature have been recorded since Sir B. Brodie's famous case of injury to the cervical portion of the cord observed in 1837, when the temperature was 111°. After fracture of the cervical or sometimes of the dorsal vertebræ temperatures ranging up to 110° or more have been observed.

In some the temperature reached its highest point immediately before, or even after, death, as in a case reported in *St. Thomas's Hospital Reports* (vol. i. p. 493) in which the axillary temperature after death was 110°. Teale's case has already been spoken of.

In another series of cases, similar injuries have produced a fall of temperature. Mr. Hutchinson has recorded a case of fracture of the fifth cervical vertebra, where the rectal temperature fell to 95.8°, and in a case of fracture at the first dorsal vertebra 80.6° was noted. Injuries below the first dorsal vertebra appear never to have been observed to be followed by excessive lowering of temperature. But no general law has been traced, which determines why there is sometimes a rise and sometimes a fall.

It should be remembered that *shock* is often an important element in these cases, as the injury producing the spinal lesion is often a very severe one. Besides this, we can see that in the pathological cases, as in physiological experiments, two opposing factors are at work—one, injury to the vaso-motor mechanism, causing loss of heat from the surface, and another which may be referred to the calorific nerves, causing increased production of heat. Sometimes one of these factors has the predominance, sometimes the other.

Traumatic Fever.—It has often been observed that high fever results from wounds, apparently without inflammation, or at all events out of proportion to the amount of inflammation. Numerous cases are recorded in surgical works, and only one typical instance need here be quoted. In a case of amputation of both legs for crushed feet recorded by Mr. Le Gros Clark the temperature rose from 105° seven hours before death to 110° a quarter of an hour before death, and was 110.8° after death. These cases, then, are different from the traumatic pyrexia caused by absorption of pyrogenic substances from unhealthy wounds.

Urethral Fever.—In some persons the passage of a catheter causes an immediate rise of temperature, sometimes accompanied by a rigor, which cannot be due to inflammation.

In both the last-mentioned cases it seems clear that the effect is too rapid to be due to the absorption of any pyrogenic substance from the wound or urethral surface, and that there must be some stimulus transmitted through the nerves which probably exerts a reflex action on the central nervous system. In tetanus, high, and sometimes excessive, temperatures have been observed. Wunderlich records a case where the temperature was 112.5° at the time of death. Now, although tetanus must be regarded as a specific infective disease, and, therefore, the rise of temperature may be partly due to the morbid poison, still the affection of the spinal cord and the excessive muscular contractions must be credited with part, at least, of the resulting pyrexia.

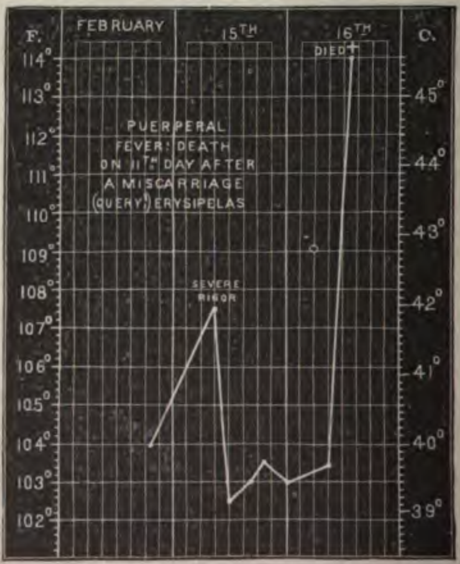
In all the above lesions and pathological states, therefore, we have evidence of the production of pyrexia from some injury to the nervous system, central or peripheral.

Unexplained Pyrexia.—A good many cases have been recorded in which there was very high temperature without any local inflammation or specific disease. Putting aside a few cases where there may have been some fraud or mistake, several remain in which there was evidently increased production of heat without any obvious cause, and where it must be supposed that there was a disturbance of the thermogenetic apparatus, either centrally or by reflex stimulation.

In several such cases the patients have been subject to hysteria. Hence, a special kind of functional thermogenetic disturbance has been distinguished, namely, *hysterical pyrexia*. Since hysteria essentially consists in functional disturbance of some part of the central nervous system, producing effects similar to those of organic change in that part, there is nothing unreasonable in the supposition that the heat-centres, like other parts of the cerebrum, may be thus perverted, though precise proof, perhaps, has not yet been furnished that such is the case.

Hysterical temperatures up to 105°, and even higher, have been recorded, but some instances of excessive temperature are open to question. Dr. Hale White gives the following as characters of hysterical pyrexia. It always occurs in girls at the age at which hysteria is most common, and the patients are often otherwise hysterical; ovarian pain and tenderness, with other symptoms, such as rigors and delirium, are often present; the temperature-variations are irregular and erratic in their course. The question requires, however, further investigation.

Fig. 25.



Sudden rise of temperature ending in fatal hyperpyrexia (Finlayson).

Hyperpyrexia.—In some febrile diseases, cases occur from time to time where the temperature, already high, rises, often rapidly or even suddenly, to an extraordinary height, without any apparent increase in the activity of the causes which had produced the existing high temperature. This condition is called hyperpyrexia. It is frequently accompanied by symptoms of cerebral disturbance, such as delirium of a low type, passing into coma, and great prostration, so that death may occur from this cause alone. Fig. 25 shows the continuous and fatal rise in cases of this kind.

This complication is most common in acute rheumatism, being formerly called cerebral rheumatism, but may occur in typhoid and other fevers, and also in sunstroke or heat-stroke. It is, in all probability, due to a direct affection of the central nervous system by the morbid poison, or whatever may be the cause of the disease; or to the exhaustion of the nervous system by a high external or internal temperature long continued. The fact that the excessive pyrexia may usually be controlled by the external application of cold makes it probable that the thermogenetic mechanism is directly implicated. Cold baths, or the application of ice, are, therefore, the recognized rule of practice in hyperpyrexia from heat-stroke, or in the other cases mentioned above.

Post-mortem Temperatures.—In some cases of hyperpyrexia the temperature not only goes on rising up to the moment of death, but may continue to rise after death. This singular fact is shown in one or two instances given above, and others might be quoted; *e. g.*, in a case of tetanus a temperature of 113° has been met with after death. If the production of heat be a function of muscular tissue, this is quite intelligible. For somatic death, or death of the body as a whole, is not synchronous with death of the parts. Muscular tissue lives (as is shown by its electric irritability) for a certain time after the heart ceases to beat, and even after removal of the muscles from the body. Hence, there is no reason why it should not perform the vital function of thermogenesis after the occurrence of somatic death.

Summary of Nervous Theory of Fever.—The facts above detailed speak for themselves. It seems pretty clear that in the instances recorded fever results from a disturbance of the thermogenic mechanism. The further question, however, arises whether, as some think, fever in general is produced in the same way. There is nothing irrational in the supposition that the pyrogenic substances which, on the zymotic theory, act by setting up chemical changes, may after all act directly on the nervous system, central or peripheral, in the same way as injuries or other lesions have been shown to do, and thus produce fever, but there is no positive proof that this is their mode of action. A word of caution may be given against any hasty inference that "nerve-force" may be converted into heat. Such a supposition is altogether premature while we know so little about nerve-force, and do not even know that there is any agency to which such a term can be applied in any accurate sense. Apparently the amount of energy travelling along a motor nerve, for instance, bears hardly a closer relation to the amount of energy liberated by the muscular contraction it causes, than the electromotive force passing along a wire used to explode gunpowder does to the intensity of the explosion produced. The same analogy applies to the production of heat.

Action of Drugs on Temperature.—Some evidence in illustration of the nervous theory of fever may be derived from the action of drugs. So far as I know, no drug has been observed to cause a direct rise of temperature except atropia. In certain cases of belladonna-poisoning a great rise of temperature has been observed, which would seem to be due to some action on the nervous system. Irritant poisons may cause a rise of temperature by setting up local inflammation, but not otherwise.

On the other hand, a considerable number of substances are known to reduce the temperature, in health to some extent, but more decidedly in cases of fever.

Such drugs are called *antipyretics*. They are divided by Dr. Lauder Brunton into two great classes: those which lessen the production of heat, and those which increase the loss of heat.

The first class he regards as acting in two ways, either by affecting the tissue-change or by modifying the circulation.

Quinine and its allies, benzoic and salicylic acids, with their compounds, alcohol, kairin, are instances of drugs the antipyretic action of which he believes to be due to their action on the tissues. They act by directly restraining the activity of protoplasm, and thus "diminish temperature by lessening oxidation. Quinine, for instance, has a remarkable influence in checking the amœboid movements of leucocytes in the inflamed tissues of cold-blooded animals, and thus hinders their migration from the vessels and restrains local inflammation. But these effects are less marked in warm-blooded animals. Quinine, however, has a marked effect in reducing a high temperature in many, though not in all, febrile complaints. In what we have specially called hyperpyrexia it appears to have little or no effect.

Production of heat is also lessened by certain drugs which affect the circulation, as antimony, salts, aconite, digitalis, colchicum. Their mode of action is not exactly determined, but it is supposed that they reduce temperature "by lessening the rapidity of the circulation through those parts of the body in which the increased tissue-change is taking place."

Antipyretics which act by increasing loss of heat do this either by dilating the cutaneous vessels and thus causing increased radiation of heat, or else by stimulating perspiration, and, hence, cooling by evaporation.

Under the first head come alcohol, nitrous ether, antipyrin and thallin. Their action must be upon the vaso-motor system, and is, therefore, analogous to that of lesions affecting the vaso-motor centre already spoken of. The action of sudorifics hardly needs explanation. But the external application of cold is, after all, the most powerful of all antipyretics. It would thus appear that pharmacologists do not recognize any antipyretic drugs as acting directly upon the heat-centres; and these drugs, so far as yet known, affect thermotaxis only, not the thermogenesis. It is, however, quite possible that some antipyretics may act through the nervous system.

Degeneration of Tissues.—Another evidence of chemical change taking place is the degeneration of the tissues which we find after the febrile process is at an end. This is particularly noticeable in the muscles, and is the more striking because during fever the muscles have for the most part been doing no work. The change in muscular tissue consists in the so-called vitreous or hyaline degeneration. The fibres swell up, lose their striation, and become translucent. This is only seen when fever has lasted for a long time, and is most noticeable in typhoid fever. It is generally regarded as a consequence of high temperature long continued. But it is, after all, not impossible that it may be a concurrent effect of the same poison as produced the fever. In glands—most noticeably in the liver—the epithelium is generally found in the condition called cloudy swelling, or parenchymatous degeneration, elsewhere described.

Concomitant Symptoms.—Besides heat and tissue-changes, the next most noticeable symptom in fever is disturbance of the circulation. The action of the heart is accelerated; so that before the introduction of the clinical thermometer a rapid pulse was the principal criterion of fever. The febrile pulse is sometimes at first rapid and hard, showing tonic contraction of the muscles of the smaller arteries. Afterward it becomes large and soft, showing that the arteries are relaxed. When the heart's action begins to fail it will be small and soft. In spite of the apparent violence of its action the heart in fever is probably always weaker than in health, and for the most part very much weaker. The arterial blood-pressure is generally, except in the early stage of certain fevers, low. This disturbance of circulation must be regarded as in some way a consequence of the increased temperature of the body, though in what way this is produced is not quite clear.

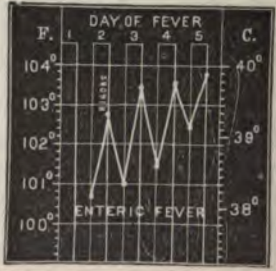
Increased frequency of respiration is an equally constant symptom of the febrile state. It may be regarded as partly a consequence of the more rapid action of the heart, but is also an evidence of the augmented production of carbonic acid and water in the tissues, resulting from the chemical changes of which we have already spoken, and the excretion of these products of combustion through the lungs.

It has long been observed that the composition of the urine is altered in fever. It is diminished in quantity, but highly concentrated and dark colored, so that it contains more urea and more pigmentary matter than normally. The amount of uric acid excreted is also greater than in health, and is often deposited in the form of urates. The phosphates are also increased.

The functions of the skin are notably affected in fever. The sensible perspiration is sometimes diminished, sometimes very greatly augmented; but it is important to remember that the insensible perspiration is always increased—that is, the dry skin of a fever patient is continually giving off much more than the normal amount of water. The nervous symptoms of fever are chiefly seen in the central nervous system. The cerebral symptoms—such as headache, excitability, hyperæthesia of the various senses, delusions and delirium—may all be regarded as showing that the brain is in a state in which the equilibrium of its substance is easily disturbed, and are doubtless evidence of a direct injury to its substance, as well as of disturbance of circulation. Whether this injury is produced merely by the heightened temperature, or whether it is the concurrent effect of the poison which produces fever, must be regarded as uncertain. Some of the symptoms, such as coma and the so-called typhoid state, so much resemble the effects of certain poisons that they may be attributed to the direct poisoning of the blood.

Clinical Types of Fever.—The febrile process usually reaches a certain height and then begins to decline. The commencement of decline, or crisis, is often marked, not only by a fall of temperature, but also by changes in the secretions. In certain kinds of fever, the crisis may sometimes be looked for at a particular date from the commencement of the disease. It was formerly thought that this was most likely to occur on one of the uneven days—that is, the third, fifth, etc. More lately it has been thought that the law of periodicity is shown by a change occurring at the end of a weekly, or even a half weekly, period, which would be on the fourth, eighth, eleventh, fifteenth day, etc., but there is little certainty in these supposed laws. The onset of fever is sometimes sudden, so that a high, or even the highest, temperature is reached on the first day. But more generally the rise is gradual, the temperature on each successive day being higher than that of the day before. A good instance is the rise of temperature at the onset of typhoid fever, which nearly always follows the typical courses, shown in Fig. 26. The evening and morning temperatures respectively are higher than the day before, though there is a daily fluctuation.

Fig. 26.

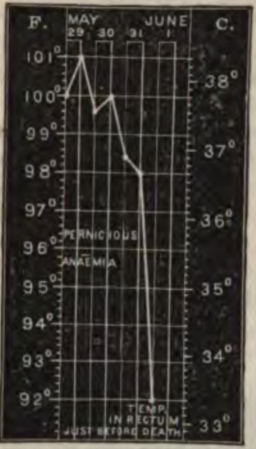


Course of temperature for the first five days in a case of typhoid (Finlayson).

A sudden fall of temperature, if not merely temporary, is called a *crisis*, as showing a decisive turning point in the course of the disease. It characterizes certain forms of fever, of which lobar pneumonia is one of the best marked instances. If the sudden fall is continued into an extremely low or subnormal temperature it constitutes *collapse*, and this is in many cases the sign of a fatal termination of the disease, as shown in Fig. 27.

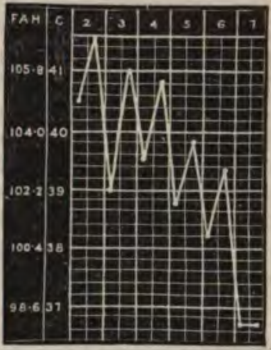
A more gradual fall, in which the temperature is lower on each of several successive days, is known as *lysis*. This mode of termination is the rule in certain fevers—for instance, in catarrhal inflammations, bronchitis, and the like, and in typhoid fever. It is shown in Fig. 28.

FIG. 27.



Fall of temperature ending in fatal collapse (FINLAYSON).

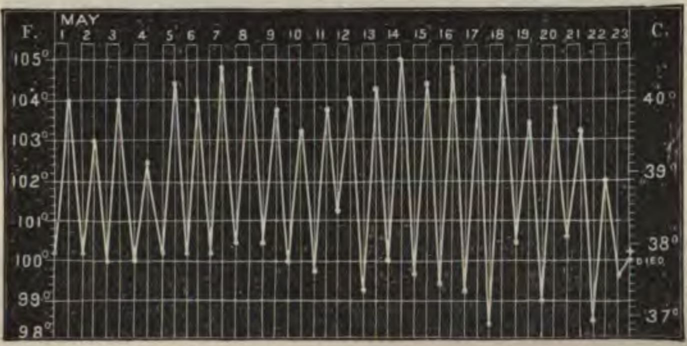
FIG. 28.



Gradual termination of fever or lysis (FINLAYSON).

Febrile temperature, for the most part, so far follows the laws of normal temperature that it is higher in the evening and lower in the morning. Deviations from this are sometimes observed, the morning fall, for instance, being omitted, so that there is a continuous rise from one day to another, or the morning being higher than the even-

FIG. 29.



Phthisis (FINLAYSON).

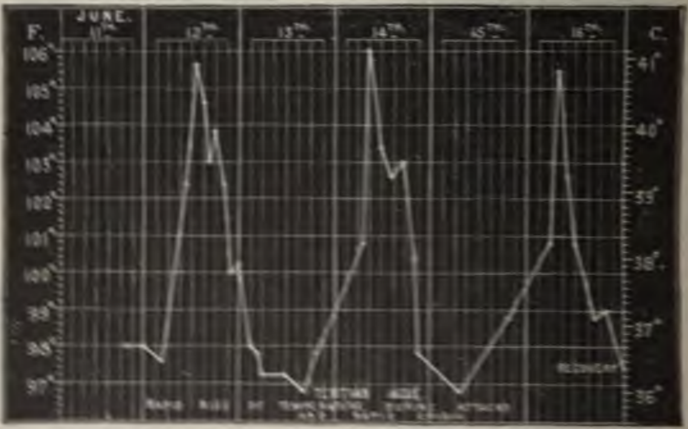
ing temperature of the day before. Such variations occurring in the course of a fever are generally regarded as unfavorable.

Fever which lasts for a long time is sometimes called hectic (which means merely *habitual*); but the word has come to be used with special reference to the fever which accompanies tubercular disease or consumption. The peculiarity of this form of fever is that the morning temperatures are often comparatively low or even normal, while there is a daily rise in the evening (*see* Fig 29).

The difference between this and the temperature in a long-continued case of typhoid fever, for instance, is that in the latter, while the fever lasts, the temperature, even in the morning, is above the normal, though lower than in the evening.

Fevers may be distinguished as intermittent or continuous. In intermittent fever or ague, a rise of temperature may occur daily (quotidian), or every other day (tertian), or even every third day (quartan). The rise is rapid, and after the acme is reached there is an abrupt fall, so that the state of the fever lasts for a part of the day only, the temperature between the paroxysms being normal. Thus in the tertian form (*see* Fig. 30) the temperature is normal on each alternate day.

Fig. 30.



Course of temperature in tertian ague (FINLAYSON).

In relapsing fever a febrile period of several days is followed by a period without fever, and then by a return of the febrile state. These distinctions will probably depend upon differences in the specific cause producing these diseases, and therefore have not any general application.

For the sake of clearness we may point out the difference between speaking of *fever* and of *a fever*. By fever is meant the general state which we have now been considering. Fevers are certain special diseases to which capriciously this name has been applied.

CHAPTER XII.

LOCAL DEATH: NECROSIS AND GANGRENE.

DEATH of the whole body, or *somatic death*, implies that the body is no longer capable of assimilating new material and converting it into living tissue. The elementary parts of the organism, when this happens, become subjected to chemical affinities, which may go on liberating energy, but not according to any definite law. They are decomposed, in fact, without any relation to one another, like a mere agglomeration of molecules; and the chemical changes are quite uninfluenced by the fact of these parts having previously belonged to a living body.

These changes are precisely illustrated by the action of gravity on a revolving body when the initial impulse of revolution is exhausted (*see* Introduction).

There is one corollary from these results which, if the truism be pardoned in consideration of all it involves, may be worth pointing out—that *a dead body is not subject to disease.*

The death of the tissue elements is not necessarily simultaneous with somatic death. Generally the body as a whole dies before its elements. In cold-blooded animals the elements retain their vitality longer than in the higher species.

Some elements doubtless retain their vitality longer than others, but such differences cannot be very easily studied in the dead body. Some notion of the comparative rapidity with which they die may be formed from the conclusions arrived at by Cohnheim as to the time during which tissue-elements retain their vitality after complete stoppage of the circulation. Brain-tissue, kidney epithelium, intestinal epithelium die after two hours' deprivation of blood; skin, bone, and connective tissue will live for twelve hours. Other experimenters have found that cutting off the blood-supply from the spinal cord of an animal for one hour causes complete destruction of the gray substance, while the white substance is preserved and may revive.

In general, specialized tissues, or, broadly speaking, parenchymatous elements, die sooner than the simple supporting tissues.

There are some special points of variation which cannot be thus explained. Thus it is well known that the right auricle of the heart retains its irritability longer than any other part of that organ when removed from the body.

The converse condition in which tissue-elements die while the body is still living is what is understood by necrosis, or, in certain circumstances, gangrene. This can only happen when the conditions of nutrition are not satisfied, which may arise from one of three causes, viz., (1) By stoppage of the circulation; (2) by direct interference with the life of the cells; (3) by a temperature which differs greatly from the normal.

1. Stoppage of the circulation may be produced by many causes, which have been already enumerated in speaking of anæmia, embolism, inflammation, etc. Two forms of obstructed circulation require, however, special mention—viz., stagnation of blood by pressure, and complete capillary stasis.

That pressure, if considerable and continued, causes death of tissues hardly needs to be pointed out, and we must regard this result as chiefly due to stoppage of the capillary circulation. Internal as well as external pressure may cause what is called "sloughing," *i. e.*, death of the skin.

Complete capillary stasis involves, as was before pointed out, drying up and thus coagulation of the blood, with local death of the bloodvessels and thus of the whole part. The issue of this process in necrosis is what chiefly makes it possible to separate it from inflammation. Supposing that stasis develops, as it often does, out of simple stagnation, there is this difference that, even if the flow of blood through the part where it was stagnant be restored, the capillaries in the area of stasis are impermeable, and necrosis results. The sudden formation of an ulcer of the leg by sloughing of the skin over a limited area where the circulation is stagnant is an instance of this.

2. It may sometimes be difficult to distinguish between the effect of certain causes, as producing stasis with consequent necrosis, or as producing the same by *direct action on the cells*. Chemical corrosives or caustics, and prolonged cold or heat, may coagulate the blood in the capillaries, and at the same time produce necrotic change, independently of this, in the tissue-cells. But it is clear, from the effects of injury on the cornea or cartilage, that the cells alone may be affected. When any cause producing necrosis acts on a part generally, some elements are affected earlier than others; generally the parenchyma before the connective tissue or vessels; the gray nervous matter before the nerve-fibres; and so on. Simple concussion may destroy the integrity of brain tissue, without any wound, internal or external, of skull, skin, or membranes.

Besides the causes just alluded to as interfering with life of cells, there is one cause which appears to have a special and directly injurious effect on cell life, namely the influence of bacteria which set up infective or septic processes. Any decomposing matters such as ammoniacal urine, putrid pus or other discharge, or dead tissue, all of which contain septic organisms, have a more or less deleterious effect on cell life. It does not follow that this effect is always fatal to the cell, because the vitality of the latter may be superior; but when septic organisms are contained in, or even in contact with, healthy tissues, there is always a possibility that the latter may suffer.

This property belongs in a greater or less degree to all pathogenic bacteria, as will be shown later on. Nevertheless, the effect here spoken of must be distinguished from the production of special disease. By inoculation of bacteria into the cornea, their *necrotic* effect has been demonstrated quite apart from inflammation.

Necrosis of tissues is immediately produced by some animal poisons, such as that of snake-bite, which seems to have a direct power of killing the tissues. It is also common in infective diseases such as typhoid fever; and though cachexia, weakness of circulation, and local congestions may have something to do with it, much must also be attributed to the directly poisonous action of microörganisms or their products.

3. *Temperature, either too low or too high*, if continued a sufficiently long time will produce death of tissues.

Extreme temperatures in either direction produce this result very quickly. According to Cohnheim the ear or leg of a rabbit introduced into a hot water at about 130°–135° F., or into a freezing mixture within two or three degrees of zero F., is, in either case irremediably killed, even after a very short time. But an exposure for several minutes to a heat of 114°–118° F., or a cold of 18° F., will produce at the worst, only inflammation; while still more moderate temperatures, 105° F. on the one hand, and two or three degrees on the other, even if they act for several minutes, produce only a transitory hyperæmia.

These instances show that the lethal effect of heat and cold on tissues is a matter of degree.

Frost-bite is a familiar instance of necrosis from cold; and the destructive effects of ardent heat or scalding water on the tissues are not less due to tissue-death, though the appearances may be different at first. When a burnt tissue "sloughs," it follows the same law as when a frost-bitten ear drops off.

Combination of Factors.—The above-mentioned three causes may be considered the most important factors in producing necrosis; but it is, of course, quite possible that they may be combined, and that, even if no one of the conditions should be completely fulfilled, two or more of them may be partially so. Thus, in a part imperfectly supplied with blood, a comparatively slight injury may produce necrosis; and tissues of extremely cachectic persons, even though the blood be circulating freely through them, will also be abnormally vulnerable.

The first is the case in senile gangrene, where the tissues are habitually anæmic from gradual obstruction of arteries, and receive barely enough nourishment for their support, so that they are nicely balanced between life and death. Under these circumstances a very slight injury, say to one toe, will cause gangrene, which may spread over a great part of the limb, though there be no absolute blocking of its main artery by any definite mass.

The second case of extreme cachexia, though combined with free circulation of blood, is seen in *noma*, or gangrene of the face or genitals in children. This is now said to be a bacteral disease, and it is certain that microörganisms are met with, but that these are such as do not grow in healthy tissues, so that the combination of the two factors, cachexia and the action of bacteria, is what really causes the disease.

The same explanation applies to gangrene after fevers, which was spoken of just now.

Is Nerve-lesion a Cause of Gangrene?—In addition to the causes mentioned, defective innervation is by many pathologists regarded as a direct cause of necrosis. The instances given are such as sloughing bedsore (decubitus) which occurs in fevers and also in cases of paraplegia, where there is loss of motility and of sensation in the lower part of the body. The rapid onset of this symptom when the spinal cord is directly injured by fracture of the vertebræ, even in young persons paeviously healthy; and the remarkable fact of a unilateral injury to the cord becoming complicated with sloughing on the opposite side only, the part in which anæsthesia occurs under those circumstances, seems to point to some direct influence of the nerve-centres. The symptoms may appear on the second or third day after the injury, but more generally on the fourth or fifth. In the unilateral cases they may begin on the eleventh to thirtieth day.

The same symptom often occurs in acute myelitis, and more rarely in brain-disease or injury, whether unilateral or central.

It is to be noted that this affection always begins in parts of the body exposed to pressure, where the skin is drawn rather tightly over bone; and which are already in most cases anæsthetic as well as motionless; *e. g.*, the sacrum, nates, heel, angle of scapula, vertebral spine, elbows, etc. Although from these parts the lesion may spread to a certain extent, it never passes over to any quite different region of the body.

In addition to the above-named predisposing causes of malnutrition, we have to take into account the sinking down of the blood, which produces hypostatic congestion (*see* Hyperæmia, p. 42) when the heart is weak, the feebleness of the circulation generally, and, further, the frequent complication with septic or infective disease.

Considering that these powerful concurring causes are all in operation at the parts affected, it seems hardly necessary to suppose that there is, in addition, any special *trophic* change set up by the nervous system. But that the condition of the central nervous system may, through the vaso-motor nerves, produce paralytic hyperæmia and so coöperate with the other causes in producing gangrene, is much more probable.

Another lesion supposed to show necrosis from impaired innervation, is perforating ulcer of the foot; about which we can only say here that it differs much from the other changes described as gangrene or necrosis. It is not uncommonly observed in certain diseases of the spinal cord, more especially in tabes dorsalis. A similar affection has been described by Mr. Sutton in the foot of a civet cat, in which case there was found to be profound degeration of the spinal cord in the dorsal region, and sclerosis with atrophy of nerve-tubes in the chief nerve of the limb. The evidence for a neurotic cause appears stronger than in the case of bedsore.

Symmetrical gangrene, or Raynaud's disease, is clearly due to cutting off the blood supply, and has been spoken of under Anæmia.

Another cause of gangrene is ergotism, already referred to as an instance of interference with nutritition by cutting off of blood-supply through arterial contraction. The changes which occur appear to be somewhat complicated, and to affect other bloodvessels as well as the arteries. Hence these changes also have been referred to a disturbance of the nervous system; but, after all, it seems clear that interference with the blood-supply is the immediate factor in the production of this form of gangrene, even if we suppose the vascular disturbance to be caused by abnormal innervation. Diabetic persons are liable to gangrene, the precise cause of which is not quite clear.

Varieties or Kinds of Necrosis.—Using necrosis as a general term for local death, several varieties are distinguished.

By *gangrene* is generally understood a condition of actual decomposition in consequence of death of the part. *Mortification* is synonymous. It is usually putrefactive.

Superficial gangrene covering an inflamed part is *hot* gangrene, in distinction to cold, or *sphacelus*, which extends more deeply and widely. *Moist* gangrene is actually putrefactive, while in the condition called *dry* gangrene, or mummification, there is a slow drying up of the tissues into a mass which may remain for a very long time unchanged. The chief predisposing condition is evaporation, when this is possible from loss of the epidermis.

Spontaneous gangrene is a term of doubtful propriety, meaning, rather, *sudden*.

Inflammatory gangrene is death of a block or mass of tissue in consequence of inflammation.

Hospital gangrene is a disease affecting wounds, is transmissible from one person to another, and caused by microörganisms.

Necrosis, as distinguished from gangrene, has no special name, though it might be well if it had, since the process is very distinct. In gangrene we see in the affected part the same changes as we see under different circumstances in dead bodies. They are accompanied and caused by the presence of microörganisms, except in the case of mummification. The changes in simple necrosis, as seen in internal parts, may be referred to the cells chiefly, and partly to the smaller bloodvessels.

Process of Necrosis.—When a cell dies, its protoplasm undergoes certain changes which are closely related to coagulation of fibrin, or to rigor mortis in muscles.

In coagulation of blood or lymph the *death* of leucocytes is thought to liberate the fibrinoplastic substance and the ferment which, with the fibrinogenous substance of the plasma, form fibrin.

Now, according to Weigert, there occurs in the death of tissue-cells a process which is in a certain sense the converse of this, and has been called *coagulative* or *hyaline necrosis*. There is coagulation, which takes place within the cells, instead of outside them, as in coagulation of blood. The cell becomes penetrated by the lymph, which contains a fibrinogenous substance. With this, the fibrinoplastic substance of the cell combines, and coagulation results, producing a stiffness or rigidity which is analogous to rigor mortis.

The first noticeable change is that the nucleus disappears in a few hours or a few days. Then the whole cell becomes more homogeneous, and finally breaks up into detritus.

This change is seen very clearly in an infarction of the kidney, if it is not too much tinged with blood. The color of these infarctions is so strikingly different from that of the kidney-substance, that they used to be regarded as masses of fibrin; but in sections there is at first sight very little abnormality to be seen. The substance looks hyaline, the outlines of the cells indistinct; and if different stages can be followed, the changes above described can be traced.

Hyaline (or waxy) degeneration of muscular tissue, which occurs in many morbid conditions, is thought to be essentially the same process.

In diphtheritic and croupous false membranes, the fusion of cells which have undergone this change forms homogeneous masses, often having the appearance of fibrinous exudation from the bloodvessels.

Recklinghausen describes a "hyaline thrombosis" of small arteries, in which the hyaline masses result from the fusion of fibrin and the blood-elements. He has seen this very widely spread through masses of necrotic tissue, in senile gangrene and other conditions. The smaller vessels are filled with this hyaline material, and sometimes arteries of a recognizable size also. He regards it as a cause of necrosis, especially in cases of "spontaneous senile gangrene" where there is no obstruction of large trunks. Very similar appearances have been described by Dr. Handfield Jones, in cerebral arteries (*Trans. Path. Soc.*, vol. xxxv. p. 134).

Termination of the Necrotic Process.—In necrosis, unaccompanied by putrefaction, there are two possible issues to the necrotic process. If the amount of liquid be abundant, as is the case, for instance, in the brain, the tissue liquefies—that is, breaks down into a thick fluid containing disintegrated materials. The softening of thrombi and infarctions, and that which less commonly occurs in lymphatic glands after inflammation, are other instances. The requisite conditions are—prevention of evaporation and imperfect removal of fluid by the lymphatics.

If the fluid be deficient, so that the necrotic masses are very dry, the so-called *caseous* change results. This is seen when large masses of cells press upon one another, and undergo necrosis, while the fluids are removed by the lymphatics. Collections of leucocytes in lymphatic glands from chronic inflammation or tuberculosis undergo this change. It seems as if the lymphatics were able to carry off the fluids, but not the cells, so that the latter are left behind, as if on a filter. Cellular productions, such as the products of tubercular inflammation, and syphilitic masses, undergo the same change. The yellow, crumbling appearance is partly due to fatty degeneration of cells.

It is not necessary to suppose that the death of cells, which is the starting-point of this process, is caused directly by their mutual pressure. It is more probably due, at least in the specific inflammations, to the directly poisonous effect of the specific virus, whatever that virus may be.

This process of dry necrosis or caseous change generally, if not always, ends in calcification, provided no other change supervenes. Thus are produced the calcareous masses which, as before pointed out, form the last stage of many inflammatory products. But there may be a great deal of calcareous change, even when the resulting mass is not quite solid, for the gruel-like pulp of degenerated lymph-glands often contains calcareous granules.

Separation of a Necrotic Mass.—Every mass of necrotic tissue, whether distinctly gangrenous, or the result of hyaline necrosis, becomes isolated from the rest of the body. This isolation is effected by inflammation.

In external gangrene, a well-marked zone of suppurative inflammation may be seen dividing the sound from the gangrenous tissue. The normal or healthy result of this is that the dead mass is cut off from the living body.

In internal parts the process is rather different. The inflammatory zone is always seen when the necrosis has advanced to a certain stage, but it does not necessarily suppurate. The hyperæmic tissue becomes infiltrated with leucocytes, and ultimately a band of fibrous tissue is formed, which may have the distinctness of a capsule. The walls of this capsule must have some power of absorption, as a great part, sometimes the whole, of the necrotic mass may be removed and only a fibrous scar remain. Sometimes a residue is left, which becomes calcified.

Thus we see the organism treats a dead part as it deals with a foreign body. If possible, the foreign body is eliminated by suppuration. If not, it is surrounded by a fibrous capsule, and rendered inert.

The process of incapsulation is essentially the same, for instance, around a parasite, a dead syphiloma, a dead mass of tubercular matter, or even a piece of dead bone.

The after-differences depend upon whether the included mass is capable, or not, of being expelled; or whether the injurious part of it is capable of being absorbed. The fibrous capsule of an abscess appears to have the power of carrying away what is injurious in an abscess, so that, while at first it infects the organism with a fever-poison, afterward it ceases to do so. This removal is effected by the lymphatics of the fibrous tissue.

The reason why a piece of dead bone, for instance, refuses, so to speak, to become incapsulated, and maintains an open sinus from which pus discharges, is that the part contains septic microörganisms. These prevent the formation of healthy tissue, and it is a favorable circumstance for the organism that they do prevent it, for otherwise dangerous materials would often be retained within the body. A perfectly aseptic fracture heals up without a sinus, as is well known from the results of antiseptic surgery, and from the experiments of Hueter and others.

CHAPTER XIII.

ATROPHY, GENERAL AND LOCAL.

THE word atrophy, which means literally want of food, is used to signify the result of such a privation, namely, wasting or diminution in size. It implies partial, not total, deprivation of nourishment; since the latter produces general or local death (*necrosis*). Strictly, moreover, the word does not apply when there is a qualitative change as well as a quantitative. But since many processes which are at first alterations of quality (degenerations) lead in the end to diminution of size, it is difficult to draw the line.

Atrophy may be *general* or *local.*

General Atrophy or wasting of the whole body, may be due to want of food, or to some condition interfering with the absorption and assimilation of food.

The most perfect example of general atrophy is seen in slow starvation. But cases in which the organs of digestion are seriously affected, such as obstruction of the pylorus by cancer, are cases of virtual starvation.

Many diseases which cause wasting of the body were formerly known as "Consumption," or, in Latin, "*Tabes*"; but, by a singular limitation of use, the former of these terms is now exclusively applied to a disease of the lungs, the latter to a disease of the spinal cord. The wasting of old age is a form of general atrophy.

General atrophy, from whatever cause, affects different tissues and organs of the body unequally. The adipose tissue is first subject to wasting, then the muscles, then the internal viscera, last of all the brain and the skeleton. All atrophies produced by want of nourishment follow the same law, and are thus distinguished from the special forms of atrophy in which one system, such as the muscular, is preëminently affected. The atrophy of old age affects especially the skeleton, the skin, and the nerve-centres.

Atrophy affecting children is sometimes distinguished as a special form, under the name of infantile atrophy or marasmus, and is often ascribed, on very inadequate grounds, to disease of the mesenteric vessels, as tabes mesenterica or "consumption of the bowels." Infantile atrophy is really no distinct malady, but the result either of improper food, or of some chronic disease of the digestive organs, or of some general disease.

The causes of general atrophy in adults are too many and various to be here enumerated.

Local Atrophy.—Atrophy, or smallness of any part of the body, may depend upon a congenital condition or may be acquired.

Congenital atrophy—more accurately called congenital smallness—is the condition in which some part of the body, through arrest of growth, never reaches its normal size.

This condition sometimes affects the whole of one side of the body, so that the two sides are unequal, when it is called *Hemiatrophy*.

Such an inequality may evidently be produced also by hypertrophy of one side, but in practice there is little difficulty in distinguishing the two conditions; the atrophic side being shown to be the abnormal one by special wasting or muscular weakness, sometimes by actual hemiplegia.

Atrophy of the limbs and trunk on one side is sometimes accompanied by atrophy of the same side of the head and face, but more generally by that of the opposite side. This latter condition, which may be called transverse or cross atrophy, points unmistakably to a unilateral affection of the brain, either congenital or beginning in very early life. In a certain number of such cases, evidence has been given of injury to the brain at birth, through delivery by forceps. In some cases idiocy or defective intelligence has been recorded, in others the cerebral functions were normal.

Hemiatrophy, affecting the head and face only, is more common than the last named condition, and is known as *hemiatrophia facialis*. It may be congenital, or may come on in childhood or adult life. In the latter case it is often progressive, the skin being first affected, then the soft parts and then the bones, so that ultimately the whole affected side of the head is measurably smaller than the other, and the corresponding half of the tongue smaller than the other. The ears, in some cases at least, show an analogous inequality. Sensation is sometimes lost, sometimes unimpaired. The special senses are mostly somewhat impaired in their function; but not necessarily affected by any lesion. Muscular paralysis is no part of the affection, though the muscles will be wasted. The affected side is usually more or less anæmic as compared with the other, but the control of the sympathetic nerves over the circulation is at least in some cases preserved.

There can be no doubt that this form of atrophy is essentially caused by an alteration in the nervous supply of the part; and the negative characters given above evidently exclude the facial and the cervical sympathetic, so that the symptoms are clearly referable to a lesion of the fifth nerve. The absence of cerebral affection, and certain other definite facts, also prove further that this nerve is affected after leaving the brain, either in its trunk, its branches or in one of its ganglia.

The conclusion to be drawn from these facts is that this mainly sensory nerve has a direct relation to the nutrition of the parts to which it is distributed. It has a tropic function, in addition to its other functions. This result has an important bearing on the explanation of other forms of atrophy where the nerves supplying the parts are mixed nerves, and their functions cannot therefore be so well discriminated.

Some other forms of atrophy may be also traced to faulty innervation. The atrophy of paralyzed muscles is partly due to simple *disuse;* but this is not an adequate explanation in all cases, since the amount of wasting varies very much in different forms of paralysis. In the so-called infantile or essential paralysis due to anterior poliomyelitis or inflammation of the anterior gray cornua (in adults as well as children), atrophy of the affected muscles is very rapid, and of an intensity quite disproportionate to the mere inactivity of the limbs. In progressive muscular atrophy, though caused by disease of the spinal cord, wasting of the muscles is the most marked feature, and precedes paralysis. These diseases plainly show an impairment of the trophic function of the nerves, independent of the loss of motor power. In various other spinal diseases, as glosso-labio-pharyngeal paralysis, the atrophic element is present: combined in various degrees with motor and sensory defects, and, where not simply the result of inactivity, is evidence of the same alteration in the trophic functions. We cannot here consider whether this function is located in any special part of the nervous system.

Atrophy of the testicles has been in several cases observed as a consequence of injury to the spinal cord, brain, or cerebellum. An injury of the cord producing paraplegia, if in the region of the lower dorsal or upper lumbar vertebræ, will, according to Klebs, constantly produce, in one or two weeks, a softening of the glands, resulting in atrophy, and accompanied, after a time, by complete absence of spermatozoa. Similar results have been produced experimentally in animals by section of the spermatic nerve.

The remaining special causes of atrophy may be classified as (1) disuse or in activity, (2) overuse, (3) pressure, (4) deficient blood supply, (5) destruction of the tissue-elements by inflammation or specific poisons.

1. **Atrophy from Disuse** is seen in all organs which have a constant active function, when this function is interrupted.

Organs whose functions are periodic do not suffer in the same way, or scarcely so. This is seen in the sexual organs, the functions of which may remain in abeyance for long periods of time without wasting; most conspicuously in the mammary gland, which, though it is called into functional activity only for a short time and with long intervals of rest, remains ready to respond to the functional stimulus when that comes into operation. But after the climacteric period, when pregnancy is no longer possible, the apparatus of lactation undergoes atrophy. There is no sufficient evidence of the assertion sometimes made that rigorous celibacy in men is followed by wasting of the testicles. At least, if this does occur, it is only after many years.

Instances of organs with constant functions which suffer atrophy from disuse are the digestive organs, muscles, and nerves, and certain parts of bones.

When the stomach no longer takes in food, either from absolute starvation or in cases of obstruction of the œsophagus, the organ becomes extremely wasted, being sometimes apparently not larger than a piece of intestine. This can only occur when life is prolonged by nourishment introduced by another channel, as by nutrient enemata. The other digestive organs suffer also, though in a less degree.

Muscles which are cut off from connection with their motor nerves, and thus rendered inactive, undergo slow wasting. This is seen in its purest form after hemiplegia from injury to the corpus striatum, or in paralysis of a limb from nerve-section. The paralyzed muscles slowly waste, passing through the stage of fatty degeneration, and frequently ending in rigidity—a process very different from the rapid atrophy of the special diseases mentioned above.

Nerve-fibres cut off from their central connections—that is, from the ganglion cells—invariably and rapidly waste. If, for instance, the muscle-nerves in an animal are experimentally divided, the electrical irritability of the nerve is quite lost within four days, though the muscles, if directly excited, retain their irritability much longer. If healing be prevented, the peripheral portion of the nerve undergoes rapid degenerative atrophy, while the central stump remains entire. An apparent exception is found in the case of the posterior roots—namely, that the portion of the root between the spinal ganglion and the spinal cord degenerates, while that between the ganglion and the peripheral portion of the nerve is preserved. This shows that, for the motor fibres, connection with the gray matter of the cord is necessary to preserve their vitality, while the same result is attained for the sensory fibres by their connection with the ganglion.

In cases of old amputation of limbs, when nervous currents have ceased to pass for many years, more extensive changes have been observed—viz., atrophy of the nerve-trunks in the stump, of both roots of the nerve, especially the posterior, of the posterior white column of the cord on the side of the amputation, and, to a small extent, of the gray matter also. These changes, however, have not been found in all cases.

The process of atrophy in nerve-trunks is effected by means of the fatty degeneration elsewhere described (*see* Chapter XIV.). It is accompanied or followed by inflammatory and other changes in the neurilemma, but these are probably secondary.

Even bones also undergo atrophy from disuse, that is, when not maintained under the normal mechanical conditions. The long bones of the limbs become smaller, not only when the limb is paralyzed, but when it is kept for a long time immovable through pain. In cases of dislocation the socket of the joint wastes when it no longer holds the head of the bone. The alveolar process of the jaw, from which teeth have fallen out, wastes and is absorbed when the pressure of the teeth is removed.

2. **Atrophy from Overuse.**—Overwork is less commonly a cause of atrophy than underwork; nevertheless, a certain number of cases are met with where atrophy of actively functioning organs occurs from this cause, if there be at the same time imperfect nutrition. It is seen in the nervous, muscular, and secreting systems.

a. Nervous system.—From what has been said above of the relative liability to atrophy of different tissues, we should expect that the ganglionic nerve-tissue would suffer first; and it is thus that we must explain the undoubtedly injurious effects in certain cases of excessive cerebral activity. Symptoms of loss of control or over-excitability are, perhaps, the first evidence of impaired nutrition of the cerebral cortex; next, diminished power of performing the functions which have been unduly exercised, or what is called loss of intellectual power; finally, complete functional incapacity, or amentia.

It is also highly probable that some of what are called the systemic diseases of the spinal cord result from the overwork of particular nervous tracts, though there is at present hardly adequate anatomical evidence for this conclusion.

In the case of complicated movements, which require for their performance a special combination of the nervo-muscular mechanism, we see also similar instances, as in the class of hyperkinetic diseases, represented by writer's cramp. In some cases (usually as early symptoms) we see tremors or cramps, indicating imperfect nutrition or degeneration of the nerve-centres. In more extreme cases, or in later stages, we have failure of the conducting nervous system, or motor-paralysis, and finally wasting away of the muscles.

But in all cases of nervous atrophy thus produced, the most important determining factors are—insufficient intervals of rest interfering with the nutrition of the body as a whole.

b. Muscular system.—Muscles rarely become atrophied from overwork, but instances are known, especially in cases where the body generally is badly nourished. I have seen a porter in whom, as the result, apparently, of carrying excessive burdens on his shoulders, there was symmetrical atrophy of certain muscles, especially the trapezius, supraspinatus, and infraspinatus, the deltoids being unaffected. Although of robust build, the man had been for a long time half-starved.

The commoner kind of progressive muscular atrophy affecting the shoulder and one arm of one side has also, though with less probability, been referred to overuse, on the ground that this affection is most often seen in the laboring classes, affects men more often than women, and the right arm more often than the left. Rapid atrophy of muscles has been said to occur in soldiers when badly fed, after long, exhausting marches.

The heart, though generally enlarged by increased work, shows atrophy, taking the form of rapid dilatation, as a consequence of violent exertion, without proper preparation, or with insufficient food. I have often seen cases of this "acute cardiac dilatation" in youths with insufficient physical power employed in engineering works, and using hammers of great weight.

c. Glands.—It can hardly admit of doubt that premature wasting of the testicles results, in some cases, from sexual excesses.

3. **Atrophy from Pressure.**—In contrast to the last-mentioned instances, we find that pressure is in many cases a cause of atrophy.

For this the pressure must be constant; if intermittent, it causes hyperæmia and often hypertrophy as before shown. The instances of wasting of soft tissues and solid structures, when pressed upon by aneurisms or other tumors, are too familiar to need description.

External pressure will often cause wasting, provided it be not so severe as to cause actual death to the part, or necrosis.

4. **Atrophy from Obstructed Blood-supply.**—This may of course occur, but is not in practice a very common cause of wasting, since some more complex changes, such as necrosis or infarction, are generally set up by arterial obstruction. In many cases wasting of an organ and narrowing of its arteries go hand in hand, without our being able to say that one is the cause of the other. This is partly the case in senile atrophy; nevertheless the wasting of special organs in old age, as the skin, the spleen, and the kidneys, seems related to the gradual obliteration of arteries which is characteristic of advanced life.

We sometimes find *post-mortem* a kidney wasted from obstruction of its artery, probably through an embolism which blocked it a long time previously.

5. **Atrophy from Inflammation.**—In all inflammations there is some destruction of tissue-elements; and it often happens that the loss thus caused is never reinstated, so that permanent atrophy of some tissue or tissues results. This is seen, for instance, in inflammation of muscle, where the muscular tissue is never completely restored; and in secretory glands, where the gland-cells suffer atrophy if the organ is inflamed. The same is true of the brain and other nervous tissues.

On the other hand, it is possible that the processes of repair which follow inflammation may predominate over destruction, and hypertrophy be the result, as in fibrous tissue and bone.

Certain special poisons appear to cause atrophy of special tissues; for instance, lead-poisoning produces wasting of certain muscles. So it is asserted that iodine may cause atrophy of the thyroid, mamma, and testicles; but this requires confirmation.

Unexplained Atrophies.—It must be admitted that some atrophies cannot be explained by any of the causes enumerated above. Some are phases of natural development, such as the wasting of the thymus in early life, and that of the mammæ and sexual organs at a later age. But in others no such explanation can be given. The skin sometimes wastes in certain definite directions, producing the so-called *linear atrophy*, which though it may be a consequence of pregnancy, or of obesity, occurs also in the absence of either of these conditions. In the very rare disease called *muscular atrophy*, the same lesion is found in spots or patches instead of lines.

Bones sometimes undergo a peculiar form of atrophy, rendering them brittle (*fragilitas ossium*); but this condition, though causing undoubted waste of the bony tissue, is apparently dependent on changes in the medulla, which are rather hyperplastic or inflammatory.

CHAPTER XIV.

ALBUMINOUS AND FATTY DEGENERATION.

By degeneration is meant a change for the worse in some part, tissue, or element of the body, regarded with reference to its quality. It is not degeneration when a part is curtailed, maimed, or wounded: nor when it actually dies (*i. e.*, becomes gangrenous); but it is so when the subject becomes changed into something less highly organized, less complex in chemical composition, or less suited for the performance of the proper functions of the part.

Tabular View of Degenerative Processes.

Name.	Nature of process.	Parts affected.	Cause.
Albuminous.	Metamorphosis.	Muscle, epithelium.	Fever?
Fatty.	Infiltration.	Connective-tissue, gland-cells.	Imperfect oxidation.
Fatty.	Metamorphosis.	Muscle, gland-cells, etc.	Atrophy or necrosis.
Colloid.	Metamorphosis.	Gland-cells, new growths.	Unknown.
Mucous.	Metamorphosis.	Epithelium, connective-tissue, new growths.	Unknown.
Calcareous.	Deposit.	Anæmic and atrophic tissues.	Special chemical reaction.
Pigmentary.	Deposit.	Normal situations: seats of hemorrhage.	Natural process: hemorrhage.
Lardaceous.	Infiltration?	Bloodvessels and fibres.	Prolonged suppuration, et
Fibroid.	Substitution.	Stroma of solid organs.	Chronic inflammation

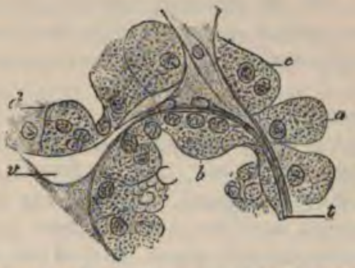
Strictly speaking, degeneration should be a chemical transformation, or *metamorphosis* of the material into some simpler chemical form: but the term is also used more loosely of processes by which some new material is *deposited* in or *infiltrated*, that is, *soaks* through the tissues or when a newly formed tissue, of inferior organism to the original, replaces, or is *substituted* for it.

Hence a degenerative process, in the wide sense, may be a metamorphosis, a deposit, an infiltration, or a substitution. The preceding table shows the chief degenerative processes as thus defined.

Albuminous or Granular Degeneration.—This name is given to a condition of anatomical elements, especially muscular fibres and epithelial cells, in which they are found somewhat swollen, opaque or cloudy, and filled with minute refractive granules. The general appearance is not unlike that of fatty degeneration. The distinction is that the granules in the condition now mentioned are albuminous, and dissolve in acetic acid. The organs affected appear enlarged from the swelling of their elements, pale and opaque.

This condition, also known as cloudy swelling or parenchymatous degeneration, and called by Virchow parenchymatous inflammation, is met with in many febrile diseases, especially the specific infective fevers and pyæmia; also after poisoning by phosphorus, arsenic, or strong mineral acids.

FIG. 31.



Granular swelling of renal epithelium in a case of typhoid fever with albuminuria (CORNIL AND RANVIER).

In some cases (*e. g.*, in diphtheria and scarlatina) it may be found even when the disease is of very short duration. The kidneys and liver are the organs most often examined; the muscular tissue of the heart shows similar changes, and the other muscles also, if examined, will be found degenerated.

It should be remembered that the protoplasm of all cells after death becomes cloudy and somewhat granular. The change now spoken of is, however, more marked than the ordinary post-mortem, granular condition, and, moreover, is distinguished by causing swelling of the elements.

Cause of Granular Degeneration.—The association of this change with febrile and inflammatory conditions led at first to the supposition that it represented the first stage of inflammation, and it was hence spoken of as parenchymatous inflammation. There is not necessarily inflammation of any other tissues in the organs affected, or vascular hyperæmia; and the change appears to be passive rather than active. Nevertheless it must be regarded, in many cases, as resulting from the action on the epithelial or parenchymatous elements, of the same injury which, acting on the vessels and connective tissue, produces hyperæmia, exudation, and cell-diapedesis.

There appears to be an accumulation of some kind of albuminous substance in the cell, and imperfect removal, which may be a consequence of the hyperæmia attendant on inflammation, or may be the direct consequences of the impairment of the active life of the cell caused by injury.

Another supposition is that these molecular changes are a *consequence* of the high temperature to which the tissues are exposed in febrile conditions. Though experiments have not positively established this hypothesis, there is nothing definitely to contradict it.

Fatty Degeneration and Infiltration.—These processes, though essentially different, are sometimes in practice difficult to distinguish from one another.

By fatty infiltration or *lipomatosis*, we mean the excessive deposition of fat in certain cells which normally contain some; that is, in those situations in the body where fat is normally accumulated.

These situations are: (1) areolar connective-tissue, especially that under the skin and that surrounding certain abdominal viscera: the omentum, and that which separates muscular bundles both of the heart and voluntary muscles: (2) gland-cells, more especially of the liver.

1. This infiltration of connective-tissue with fat appears to be regulated by the amount of fatty matters absorbed by the blood, and the amount oxidized by respiration. If the former process be greatly intensified or the latter hindered, an excessive accumulation of fat takes place. Although such an accumulation is, in most instances, general, it is sometimes much more marked in certain parts of the body than in others. The causes which determine accumulation of fat at one part more than another are not well understood, but appear to be stagnation of circulation and consequent deficiency of local respiration. Thus insufficient action of the muscles leads to obesity, and as regards the heart it would seem that occasional forced action, and consequent rapid circulation, are necessary to prevent the accumulation of fat there in well-nourished persons. It is also clear that inertness or want of power in the sexual organs favors the accumulation of fat, though in what way is not known.

The process of "training" men or animals for feats of strength, supplies evidence that profuse perspiration removes excessive accumulations of fat: and trainers believe that fat can be removed from one part specially by production of local perspiration there. Internal fat is removed by increased muscular activity, leading to increased oxidation. An instance of the power of diminished oxidation to favor accumulation of fat is seen in anæmic girls in whom the oxidizing power of blood is deficient and who are generally fat though not really well-nourished.

Fatty infiltration of connective-tissue amounting to a disease is hardly known except in connection with the heart and muscles, unless general obesity be so considered.

Fatty Infiltration of the Heart consists first in the production of an unusual quantity of adipose tissue in the visceral pericardium: next in deposit of fat in the interstitial connective tissue of the heart-substance. The external fat is of little consequence. It is often seen in abundance on the hearts of persons killed by accident in robust health; and there is no reason to think that it impedes the action of the heart. Such a condition should therefore never be set down, under the name of "fatty heart," as a cause of death.

Infiltration of fatty tissue among the muscular bundles gives a yellowish appearance to the heart-substance, and renders it to some extent softer than natural. It resembles the flesh of overfed animals.

But it is most important to remember that this does not *necessarily* imply any affection of the *muscle-fibres.* The latter are affected by fatty *degeneration*, to be presently spoken of, and this condition may accompany fatty infiltration, but need not do so, and may occur independently. Hence, careful microscopical examination is necessary before we can say that there is fatty degeneration of the heart.

In the voluntary muscles, fatty degeneration is seen to some extent in the bodies of corpulent persons who have taken little exercise. Such muscles are pale, flabby, and somewhat soft. It must be supposed that they are functionally less competent than normal muscles.

A very remarkable form of fatty infiltration is seen in the disease called Duchenne's paralysis, or pseudo-hypertrophic paralysis, which is really an affection of the muscles. In this disease there is an apparent enlargement of the muscles, which are prominent and hard, but the appearance is really due to a large development of fatty tissue between the musclar fibres. These fibres are at the same time extremely atrophied, but it is at present impossible to say whether the muscular atrophy or the fatty overgrowth is the primary change.

It is also important to note that the fatty tissue in and about wasting organs often becomes increased. Thus a wasted kidney is found imbedded in a mass of adipose tissue; and, when very small, is sometimes incorrectly described as converted into a mass of fat.

2. **Fatty Infiltration of Liver.**—Whether the hepatic cells in all animals normally contain fat, is uncertain; but it is quite clear that in the human subject we never find a liver of which the cells do not contain fatty drops in larger or smaller quantity.

When the quantity is extreme we have the so-called fatty liver—large, white, and often so light as to float on water, and sometimes so soaked in fat that a small portion may be inflammable.

This condition may be produced artificially by feeding animals with oil, keeping them warm, and preventing muscular movement, as is seen in the geese of Strasburg, whose livers furnish the celebrated pies. There can be no doubt that most if not all the fat is carried to the liver by the portal vein and imperfectly removed by the hepatic.

The same results are produced in a less degree in persons who take excess of fatty food, with imperfect oxidation. It is especially noticeable in alcoholic excess, probably because the alcohol suffers oxidation instead of fat.

It is more difficult to explain the occurrence of fatty liver in pulmonary phthisis and even in some other wasting diseases. The probability is that by the process of emaciation (the machinery of which is not well understood) fat is absorbed from other parts of the body, and put in circulation through the blood. but owing to the deficient oxygenation in the lungs and venous congestion of the liver, it is arrested and accumulates there.

Fatty Degeneration.—In this condition fat is formed in the substance of the tissue-elements, *i. e.*, in the protoplasma of cells, the walls of bloodvessels, etc., without being brought by the blood. Such a formation of fat can only be the result of a chemical decomposition, breaking up of the albuminates into fat and some nitrogenous substances simpler than albumen. There can be no doubt that such a process is chemically possible, since the complex molecule of albumen contains nitrogen, carbon, hydrogen, and oxygen, while fats consist of carbon, hydrogen, and oxygen only. Moreover, facts such as the following are adduced to prove that it actually occurs.

The formation of *adipocere.* This name is given to a fatty substance sometimes formed after death in the bodies of men and animals if they are kept at a low temperature in a moist place. This white, waxy-looking material may replace muscular, connective, and other tissue in such quantity as to show that it cannot be merely the fat originally contained in those tissues. Hence it is concluded that it has been formed by chemical transformation from albuminates.[1]

In the change called "ripening" which occurs when cheese is kept, there is an increase in the amount of fatty matter in the cheese, which can only take place at the expense of the albuminous constituents, since nothing is added to the cheese.

If the composition of albumen be compared with that of urea, it will be seen that the former contains a large proportion of carbon and some hydrogen not contained in the latter. Hence in the change of albuminates into urea there will be constantly set free the elements of a carbohydrate, which, unless immediately oxidized, probably remains in the body as fat.

It has also been shown that in animals fed on an exclusively nitrogenous diet (without fat) the amount of fat in the body may increase.

From these and other physiological results it is certain that fat may be formed from albuminates, and probably that the fat of fatty degeneration is thus produced by chemical change or metabolism of the protoplasm. Some physiologists are disposed to go further, and conclude that all production of fat in the body, whether normal or physiological, is due to the same cause—a subject too intricate for discussion here.

Production of Milk.—The natural type of fatty degeneration is found in the production of milk by the mammary gland. Here fatty globules are seen to be formed within the glandular epithelial cells, probably by a metabolism of its substance, when the functional activity of the gland commences. In case of the central cells of each lobule this process ends with the death and breaking down of the cells, which form the colostrum corpuscles. The peripheral cells discharge the fatty globules which form milk corpuscles, and produce others, though at length these cells are also said to perish.

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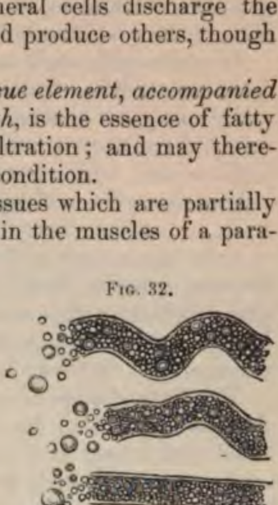
[1] The adipocere is sometimes formed in tanks where anatomical preparations are being macerated to form skeletons. This occurred in the anatomical department of the University of Oxford some years ago: but was prevented by warming the macerating chamber by gas, showing that a low temperature is the chief determining cause. Bodies buried in a damp place and thus converted into adipocere have a remarkable false appearance of freshness, and have thus given rise to the marvellous stories of corpses found undecayed after many years. In an old pamphlet entitled "Immortality in Mortality magnified," printed in 1647, is an account of a body which was found well preserved, with fat "hard as white wax" two inches thick on the abdomen, after having been buried thirty-four years, doubtless in a damp churchyard of the city of London.

The formation of fat in a cell, or other tissue element, accompanied by a process of atrophy, degeneration, or death, is the essence of fatty degeneration, as distinguished from mere infiltration; and may therefore be taken as the definition of the former condition.

Causes.—Fatty degeneration occurs in tissues which are partially deprived of vitality, or are atrophied. Thus in the muscles of a paralyzed limb, an eyeball wasted after injury, a part of the brain from which the blood-supply has been cut off—in all these and similar conditions we find fatty degeneration of various tissues. The process is, then, a consequence of malnutrition, a form of wasting, the precursor of complete local death.

FIG. 32.



Fatty degeneration of kidney-tubules in phosphorus-poisoning (CORNIL and RANVIER).

Certain poisons, notably phosphorus, produce marked fatty degeneration, first of the liver, kidney, and other glandular organs, finally of the heart and voluntary muscles. Arsenic and antimony have the same effect if their action is sufficiently intense; so also sulphuric and other acids, and probably most mineral poisons, in the ultimate and most intense stage of their action after they are absorbed. Even in chloroform and ether poisoning similar degeneration has been traced. Chronic alcoholism, which is, in fact, a slow poisoning, produces the same changes in liver, kidneys, heart, muscles, skin, etc.

These changes are attributed to interference with the oxidizing or respiratory process in the cell itself, and there are reasons for thinking that the explanation is correct. At the same time the fatty change is in so many cases the precursor of necrosis that it must be regarded as degenerative or a process tending to death. Perhaps in cells, as in complete animals, if respiration is impeded long enough, death ensues. This change is so common in certain tissues of old people that old age is loosely spoken of as the cause. Instances are: fatty degeneration of the cornea (arcus senilis), of the lens (cataract), of cartilage, especially the cells, of the connective-tissue and endothelium of arteries and capillaries, and of other parts.

Pathological products, such as cancers or other new-growths, if inadequately nourished, collections of pus if unabsorbed, blood-clots, etc., are subject to this change along with calcification.

Special Forms of Fatty Degeneration.—Fatty degeneration in muscular fibres, whether of voluntary muscles or the heart, is first seen in the muscle-corpuscles, which very commonly show fatty granules.

When the muscle-substance is affected, it becomes filled with fine granules or drops of fat, so that no transverse striation is seen. Even in extreme cases these do not run together into larger drops.

In gland-cells, such as those of the liver, it is difficult to distinguish fatty degeneration from infiltration. In fact, looking at an individual cell, it may be doubted whether there is any difference at all. Certainly the distinction of small drops (degeneration) and larger drops (infiltration), which has been alleged, does not hold in this case. The most striking form of degeneration is seen in the "yellow atrophy of the liver," in which liver-cells ultimately waste away altogether, leaving in their place only a few larger or smaller fat-drops. The real distinction consists, then, in the changes and ultimate fate of the protoplasm, which in this condition becomes destroyed, while in infiltration it is preserved, and (so far as we can trace in moderate degrees of the change) may be found still unaffected when the fat is removed.

The fatty change of renal epithelium in certain forms of Bright's disease appears to be a true degeneration, the elements becoming filled with larger and smaller fatty drops, and ultimately losing their outlines and breaking down, as may be seen in "fatty casts" found in the urine. It is also clear that their functional activity is lessened and abolished. Nevertheless the presence of a certain amount of fat is quite consistent with general health and functional activity of the organ, since some fatty drops are constantly seen in the epithelium of healthy kidneys, and the kidneys of healthy animals (cats and dogs) are often extremely fatty. It is probable that a change which begins as infiltration ends as degeneration.

When the fatty change of the renal epithelium has reached a high degree, the connective-tissue stroma also becomes affected, being filled with fatty molecules. This change is usually regarded as degeneration. At the same time it is possible that these fatty molecules may be merely absorbed from the fatty epithelium, and deposited in the connective-tissue elements and lymphatic spaces.

Fatty changes in other glands need not be here considered, since they agree with those of the liver and kidney.

Fatty degeneration of the nervous system is seen in nerves which are undergoing atrophy in consequence of being cut off from their connection with the nerve-centres.

The nerve-fibres in an atrophied nerve first show amorphous masses or drops formed by the breaking up of the medullary sheath, which after a time are changed into or replaced by fatty molecules. This change is perhaps not, strictly speaking, a degeneration, since the medullary sheath is originally composed of fatty substance.

In the brain, fatty degeneration is seen in white or yellow softening, a condition caused by sudden or gradual blocking of the blood-supply to a part of the organ. The neuroglia cells, and probably also the ganglion cells, break down into small clumps of fatty granules called granule-cells or corpuscles, formerly regarded as the sign of inflammation. Some of the granular corpuscles are probably degenerated leucocytes, or leucocytes which have absorbed fatty granules.

The rest of the tissues softens into a sort of pulp or thick fluid, containing many fatty molecules—in fact, a sort of "pathological milk."

Fatty degeneration of cartilage is very common in old age, making the substance yellow and soft. This is the cause of the softness of the costal cartilages in very old people, in whom they might be expected to be ossified.

Fatty degeneration is one of the factors in caseation or cheesy degeneration described elsewhere (p. 142).

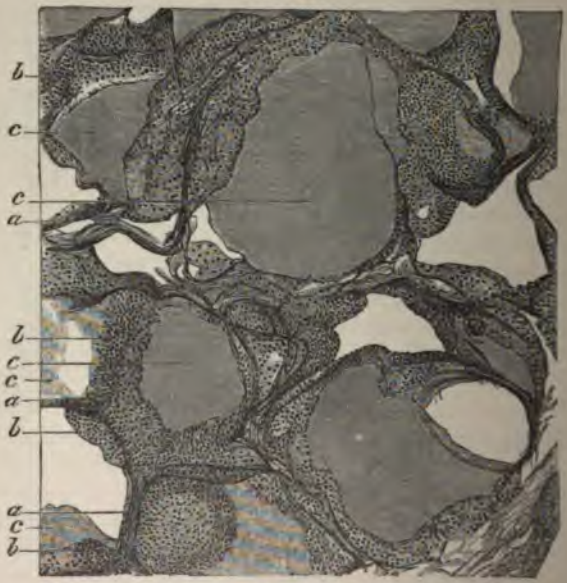
CHAPTER XV.

COLLOID AND OTHER FORMS OF DEGENERATION.

COLLOID degeneration is characterized by the formation of a translucent gelatinous substance, firmer in its consistence than mucin. I is a process chiefly, if not entirely, affecting epithelial cells.

The chemical composition of the substance is not accurately known but there can be little doubt that it is generally a mixed substance containing mucin and albuminates in variable proportions. Sometimes no mucin can be detected. Hence, probably, different chemical substances are called by the same name, as having the same physical properties.

FIG. 33.



Colloid degeneration of thyroid gland.

a, stroma separating the normal vesicles; *b*, normal epithelium, of which the nuclei only are distinctly shown; *c*, colloid masses resulting from metamorphosis of epithelium.

The physiological type of colloid change is seen in the thyroid gland. The epithelium lining the vesicles of this body secretes a hyaline substance which fills the cavity, and ultimately assumes the physical characters called colloid. This substance contains no mucin

When the gland is enlarged and degenerated, in the condition called bronchocele, colloid masses fill the enlarged vesicles, so that it must be concluded that the epithelium has undergone transformation into colloid substance. It is here difficult to draw the line between physiological and pathological conditions.

The colloid change is chiefly seen in new-growths. In compound ovarian cysts, colloid masses often fill the separate loculi. This colloid substance has been found not to contain mucin.

A certain form of cancer—colloid cancer—is remarkable for the metamorphosis of its cells into colloid masses, so that the whole has a gelatinous consistence. The stroma is unaffected. This substance contains mucin with albuminates.

In certain degenerative conditions of the kidney small cavities or cysts are found filled with a gelatinous substance. But there is little reason for connecting this with other colloid changes, except in so far that the masses are probably partly composed of degenerated epithelium.

Mucous Degeneration.—The type of this change is found in the secretion of muciparous glands, such as the salivary, where mucin is formed by metabolism of the protoplasm of the gland-cells, and set free by the breaking down or emptying of these cells.

Salivary corpuscles are cells which have undergone mucous degeneration.

The substance produced—mucin—is characterized by its transparency and viscidity, and further by being coagulated by acetic acid without being re-dissolved by excess.

In epithelial and glandular structures this form of degeneration occurs during inflammation, as an excess of the normal process, but hardly as a distinct morbid process.

In the connective tissues it is of greater importance.

Cartilage softens by mucous transformation of its intercellular substance, sometimes almost liquefying, with formation of cavities. This is seen in the intervertebral cartilages in old age.

Areolar connective tissue, in which the albuminous intercellular substance is replaced by a mucoid substance, constitutes *mucous tissue*, of which the umbilical cord is the type. This change hardly occurs except in embryonic life, when the mucous tissues are formed; but in the disease called myxœdema there is generally an excess of mucin in the subcutaneous tissue.

Myxœdema.—This remarkable disease can only be briefly noticed. Sir William Gull, who first observed it, described it as a "cretinoid condition of adult women." It is almost peculiar to the female sex, and to middle life, but some few cases in men have been observed. The chief character during life is a peculiar swelling of skin and subcutaneous tissue, not influenced in its distribution by gravity, and differing from ordinary anasarca in not pitting on pressure. This produces a peculiar physiognomy, and gives a peculiar shape to the hands, which have been described as spade-like. Other symptoms are anæmia, gradually increasing asthenia, and certain nervous symptoms which cannot be described here. The most important anatomical change, and perhaps the only constant one, is wasting of the thyroid gland, often accompanied by swelling of connective-tissue in the supraclavicular spaces. The atrophy is accompanied, as is often the case with the wasting organs, by increase of the interstitial connective-tissue (see below on "Fibroid Degeneration"). There has also been found after death a general increase of connective-tissue with hyaline or mucous transformation of the basis-substance in various parts of the body, such as the liver and the kidneys, outer coats of arteries, the central nervous system, and elsewhere. The researches of Dr. Ord, and the chemical analyses by Dr. Charles have shown that in some cases there is a large increase of mucin (normally present only in small quantity) in the skin; but this does not seem to be a constant feature. On this ground Dr. Ord proposed the name myxœdema, now generally accepted.

Some light has been thrown on the pathology of myxœdema by certain other conditions which more or less resemble it.

1. Cretinism is a state of imperfect mental and physical development associated either with the great enlargement or with atrophy of the thyroid gland. The variety called sporadic cretinism, sometimes seen in this country, where the thyroid is usually absent, and there are masses of fatty tissue in the posterior triangles of the neck, has a striking resemblance to myxœdema, especially in the physiognomy, as I have seen in placing cases side by side. Hence the propriety of the term first applied by Sir W. Gull.

2. Where the thyroid has been removed by operation on the human subject, a condition very similar to myxodema ensues, which has been called by Kocher *cachexia strumipriva.*

3. Experimental removal of the thyroid in monkeys has been found by Mr. Victor Horsley, to produce a similar condition, marked also by profound anæmia. After death a general increase of connective-tissue was found, with mucous transformation of the basis-substance, so that it contained three or four times the normal amount of mucin, while the fat was absorbed. The salivary glands were also enlarged, and furnished a large amount of mucin, even the parotid, which normally produces none. Mucin was also found in the blood. These results agree with the changes in Dr. Ord's cases.

From these instances it is pretty clear that myxœdema, or an allied condition, may result from absence or complete atrophy of the thyroid, however produced; and we must therefore regard this disease as a consequence of the atrophy of the organ. Cancer or other affections of the gland do not always lead to this result. The only theory suggested to explain this is that the function of the thyroid is either to elaborate mucin, or to effect further metabolism or chemical changes in it. If the former, destruction of the thyroid may be thought to lead to the assumption of its function by the other parts. If the latter—which seems more probable—then the check to the metabolism of mucin which normally takes place in the thyroid must be regarded as leading to its *accumulation* elsewhere.

Other connective-tissues rarely undergo mucous change; but, on the other hand, it frequently occurs in tumors.

Fatty and fibrous tumors are often partially converted into mucous tissue. Cartilaginous tumors are partly composed of the same; and it occurs as the exclusive material of tumors, which are then called myxoma, and which may be regarded as fibrous tumors in a state of mucous degeneration.

Calcareous Infiltration or Degeneration.—This change consists in the deposit of lime-salts in the elements either of an original tissue, or of some new growth, or of inflammatory products.

The immediate cause must be some chemical reaction between the tissue-substance and the small amount of calcareous salts normally contained in the blood or other fluids of the body. The precise nature of this reaction is unknown but it is always connected with lowered nutrition.

Physiologically, this change is seen in the calcification of structures, such as the stag's horn.

Here, in the first instance, a highly vascular substance is formed which contains no lime. The arteries become gradually obstructed. As this change occurs, and the tissues become anæmic, calcareous granules are deposited in the tissues around the vessels, which thus become infiltrated with calcareous matter.

Calcareous infiltration occurs as a senile change in the walls of arteries.

The muscular fibres of the hypertrophied middle coat often become calcified and rigid; but if the lime be removed by acids, the muscle-fibres are seen comparatively unaffected.

In the inner coat this change is associated with atheroma, and affects the newly formed material produced in that condition.

Inflammatory lymph, collections of pus which are not absorbed, the products of the degenerative (so-called scrofulous) inflammation of lymphatic glands, caseous tubercular masses in various organs, are the favorite seats of calcareous infiltration.

Old blood-clots in veins often become calcified, forming *phleboliths*, or vein-stones.

The tissues of a dead, wasted eyeball often become calcified, and sometimes true bone is formed in this situation.

Various new-growths are subject to calcification, as, for instance, the smooth-muscle tumors connected with the uterus (uterine fibroids).

Parasites of all kinds, when dead and encysted, as echinococcus or hydatid cysts, trichinæ in the muscles, etc., very often either become themselves calcified or become surrounded by a calcareous wall.

Since in all these cases degeneration, malnutrition, or even local death, is the precursor of the process, calcareous infiltration is very properly described as a degenerative process.

It is doubtful how far an excess of lime-salts in the blood is ever a cause of calcareous infiltration. Nevertheless in many of these cases, especially in senile changes, there is a simultaneous wasting of calcareous structures, viz., bones and teeth; so that a larger amount of lime-salts may be put into circulation, and thus favor calcareous deposition in the affected parts.

In rare cases the rapid absorption of bone from some special disease has been observed to be accompanied by excessive deposition of lime-salts in other parts. To this process the name calcareous metastasis has been given.

Pigmentation, or so-called Pigmentary Degeneration.—Some degenerative processes are accompanied by the deposition in the tissues of a black or dark-colored material which has been called pigment. Hence the term pigmentary degeneration has been used, but the deposition of pigment alone does not imply degeneration, hence this term cannot be regarded as accurate. Probably several different substances are called by the name of pigment; two at least may be distinguished.

1. *Physiological pigment*, *i. e.*, a black or brown granular substance contained in the "pigment cells" of the choroid, of the cutis, of the membranes investing the nerve-centres, in the Malpighian layer of epidermis, and in other parts. So far from being a sign of degeneration, the presence of this substance is generally associated with great physiological activity, as in the sense organs, etc. It is also found in new-growths, especially in pigmented or melanotic sarcoma, which will be afterward spoken of; and this is a growth possessing great powers of increase, and reproduction in other parts.

The only pathological conditions affecting this form of pigment are its *absence*, or diminution, and its *increase*. It is absent in the individuals called *albinoes*; but, as the condition is a congenital affection and not a morbid process, it need not be considered here.

Increase of the physiological pigment, in its natural situations, is found in certain diseases, most strikingly in Addison's disease of the suprarenal capsules; in a less degree in certain affections of the liver, and in cases of cancer.

The only point necessary to emphasize here is that the organs containing an excess of pigment are not impaired either in structure or function. The process, therefore, is not a degeneration, even though it be associated with a wasting and fatal disease.

The cause of this morbid pigmentation is unknown. The source of the pigment is also unknown, though it may plausibly be supposed to be a derivative of hæmoglobin.

In one curious disease, pigmentary excess and deficiency of the skin exist side by side, so that we have patches of white skin next to or surrounded by brown skin. This condition, usually called leucoderma, might with more propriety be named *Melanoleucoderma.*

Some curious instances are on record of "black sweat," *i. e.*, of the excretion by the sweat-glands of black pigment which is deposited on the skin. This extraordinary phenomenon, which would appear incredible were it not well attested, is entirely unexplained.

2. *Altered blood-pigment* deposited in the tissues is often the cause of brown, slaty, or even black color.

This depends upon the presence of some substance derived ultimately from the hæmoglobin of broken-down blood corpuscles, and is a sign of hemorrhage, or usually very numerous minute hemorrhages having occurred. The process has been previously explained (p. 53).

By this process, the skin, for instance, which has been subjected to violent scratching for a long time, or which has been the seat of chronic venous hyperæmia, or exposed to external heat, as when the legs are often scorched at the fire, may become very deeply pigmented, and the condition may precisely resemble excessive physiological pigmentation. The chief difference is that the artificial pigmentation will slowly pass away if the cause ceases to act. It is most conspicuous in old people.

Pigmentation of many organs, beginning with the spleen, and next in order the liver, is found as a consequence of ague. It is probably due to destruction of blood corpuscles.

Staining of the tissues by bile is sometimes spoken of as a pigmentation.

It is hardly necessary to point out that the deposition of foreign substances, as particles of carbon, stone-dust, iron filings, etc., in tissues such as lungs or skin, will produce a special tint or color.

So also nitrate of silver, taken as a medicine, may produce the well-known staining of the skin from actual deposit of the metal in some form. Arsenic, taken internally to cure skin diseases, often causes pigmentation of the parts affected with the eruption, and sometimes of the normal skin in other parts. But this is rather an excess of normal pigment than a special deposit.

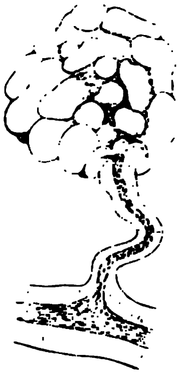
Lardaceous or Amyloid Degeneration.—This pathological change consists essentially in the presence in the tissue elements of a substance of firm, consistent, waxy lustre and translucency, and without any special color, which shows a marked resistance to chemical agents and to the action of pepsin, and also resists for a long time putrefactive change. This substance may be recognized by the colors imparted to it by several reagents. Iodine in solution gives it a reddish-brown or mahogany color, which further treatment with sulphuric acid converts into a dark—almost black—or sometimes purplish tint. Certain aniline dyes—viz., methyl-violet and gentian-violet—color the elements containing them bright red or pink, while the unaffected parts are colored blue, and thus a remarkable contrast of color is produced. Indigo solution, which does not color ordinary tissues (probably in consequence of their alkaline reaction), colors the affected elements blue.

Since the reaction with iodine and sulphuric acid somewhat resembles the action of the same reagents on starch, it was at first thought that this substance was allied to the starch or cellulose group, and on this supposition the name *amyloid*, still extensively used, was originally given to it by Virchow. The name lardaceous or bacony, previously applied to the change by Rokitansky, was derived merely from the appearance of the organs affected.

Further research has shown that the substance in question contains nitrogen, and agrees in its percentage composition with the albuminates, so that it must be regarded as a member of that group of substances, though distinguished from all other members of the group by its chemical reactions.

This substance may therefore be regarded as something formed by chemical transformation out of ordinary albumen, but how or where this transformation is effected is still uncertain. Since the change is seen in its earliest stage in immediate proximity to the blood, it might be imagined that some altered albuminous substance soaks out of the blood into the tissues. But the most minute research has never detected any trace of this substance in the blood itself, and it must therefore be concluded that it is not exuded, at all events in this form, from the vessels. The alternative supposition is that the chemical change by which the substance is formed out of ordinary albumen takes place in the elements themselves. On this ground some pathologists regard it as being produced by metamorphosis of the elements: that is, they consider the process to be a true degeneration, not, as we have called it, an infiltration. But, on the other hand, the close connection of the process with bloodvessels, the increased size of the affected elements, and the increased density of the organs affected, show that there is a transudation or infiltration from the blood, though the transuded matter may not be identical with that afterward found. Perhaps the opposing views may be partly harmonized by the supposition that there is a copious transudation of ordinary serum-albumen, and that this gives rise to a reaction with the substance of the tissue-elements by which the lardaceous or amyloid substance is deposited, just as lime-salts are deposited by a special reaction in calcifying or ossifying tissues.

FIG. 34.



Arteriole and glomerulus of the kidney in early stage of lardaceous change. (BIRCH-HIRSCHFELD.)

Seat of the Change.—The amyloid process is first traceable in the walls of bloodvessels. Those of the capillaries become thickened and homogeneous in appearance, while at the same time their lumen is narrowed. This is very obvious in the capillaries of the Malpighian tuft in the kidney (see Fig. 34). The small arteries are affected perhaps as soon as the capillaries. The change in them affects the inner and middle coat, and in the latter the muscular fibres, while the lumen is narrowed (see Fig. 34). The change is, however, irregularly distributed over the same vessel, and affects different parts of the same organ in very unequal degrees. The connective tissue is less frequently and less severely affected; gland or parenchyma cells very little, or in some organs not at all. On the whole the degeneration is one affecting the vessels chiefly, and in a less degree connective tissue. Organs affected are usually enlarged, always paler and drier than natural, being decidedly anæmic. An injection thrown into the arteries penetrates with more difficulty than in a healthy organ. The density is also increased. In advanced stages of the change there is a characteristic waxy translucent appearance, but in early stages microscopical examination and careful application of reagents are sometimes necessary to demonstrate the degeneration.

Organs Chiefly Affected.—This change is most prominently seen in the abdominal organs. The spleen appears to be the earliest affected. Here the process usually begins in the Malpighian follicles and their afferent vessels. The former become much enlarged, pale, and translucent, so as to resemble grains of sago. Hence the name "sago-spleen" is given to this condition. In a more advanced stage the whole organ is enlarged, and looks waxy from the pulp being affected in the same way. Sometimes the pulp is affected first. Next in order of frequency come the kidneys. In these organs the change always begins in the Malpighian tufts, and their apparent arterioles, which are altered in the manner above described (Fig. 34). These bodies are somewhat enlarged, and therefore more easily visible with the naked eye than usual, and have a glistening appearance. On soaking in iodine they are seen as brownish points, while the rest of the organ may be unaffected. As the change progresses the whole organ becomes waxy-looking and somewhat translucent. It is sometimes enlarged, sometimes diminished in bulk, these differences depending rather on the accompanying changes than on the lardaceous degeneration itself. In sections the degenerated epithelium and cylinders in the tubes are often found affected with the same change. In extreme cases the degeneration is widely diffused, and the basement membrane of the tubes is found thickened and waxy in appearance. I have seen the change on the surface of the pelvis of the kidney. The liver is also very often affected. In an early stage there may be little obvious change until iodine is applied, when certain portions are stained brown. The first visible effect of the degeneration is to give a translucent waxy appearance to small patches scattered through the organ, and as other portions are always found white and opaque from fatty change, a peculiar marbled appearance is produced. On minute examination it will be seen that the opaque fatty portions correspond to the outer zone of each lobule, while the translucent portion forms a broad intermediate zone, and the centre of the lobule is little or not at all affected. The translucent material is arranged in radiating masses, which at first sight have the appearance of altered liver-cells, but when carefully stained with methyl-violet are seen to be capillaries with thickened and waxy walls; so that the change is essentially in the vessels. Lymphatic glands are frequently affected, but generally only when other organs are so likewise. In slight degrees of the change microscopical examination and color reactions are necessary to establish the degeneration. There is never any great enlargement. The change affects the smaller arteries and capillaries of the glands as in other organs, and besides these more especially the reticular stroma, either of the lymph-sinuses or of the follicular structure. The lymph-corpuscles do not seem to be ever affected.

Other parts sometimes affected with lardaceous disease are the mucous membrane of the intestinal canal, and that of the stomach (though here we must beware of any fallacy arising from the color-reactions of starchy matters in the contents of the stomach).

The pancreas, supra-renals, thyroid, aorta, lungs, ovaries, and uterus have been occasionally found altered in the same way.

Isolated or local patches of lardaceous change are sometimes found in diseased tissues without any general disease. For instance, in old blood-clots, in cancers, in scars of syphilitic ulcers, in single lymphatic glands, as after typhoid fever, in fibrinous deposits on the endocardium and in the giant cells of new-growths. In these cases small masses of material are found, giving the characteristic color-reaction with iodine.

Causes of Lardaceous Degeneration.—This change is almost always found in the bodies of persons who have suffered from some cachectic disease. Pulmonary phthisis is one of the commonest antecedents. Disease of bone, especially when accompanied by suppuration, is perhaps equally common. Chronic empyema with discharge very generally leads to this condition. The above-mentioned diseases have one character in common, namely, the formation and discharge through long periods of large quantities of pus. Thus chronic suppuration is the antecedent, and presumably the cause, of lardaceous disease in the majority of cases. Syphilis is also a cause, even when this disease has not affected the bones. It has also been referred to carbuncles, chronic dysentery, and leucæmia; but instances may occur in which no cause can be traced. When the degeneration occurs in constitutional syphilis it is usually in a late or tertiary stage, rarely in the first year. But suppuration may produce the change in a few months.

Chemical Relations of Lardaceous Disease.—It has been said that parts affected with this degeneration do not give the alkaline reaction of ordinary tissues. They also differ in the amount and nature of the salts present. Dr. Dickinson, who first drew attention to these facts, supposed that there was a deficiency of alkalies generally. But the results obtained by a committee of the Pathological Society which examined this point led to a somewhat different conclusion. By analyzing the ash of specimens from three healthy and three lardaceous livers for potassium, sodium, phosphoric acid, and chlorine they found the following proportions in percentage of the liver-substance:

	Potassa.	Soda.	Phosphoric acid.	Chlorine.
Healthy livers (average),	0.2821	0.0948	0.3295	0.2073
Lardaceous (average),	0.1319	0.1902	0.1981	0.1664

From this it appears that the potassium salts are less than half the proportion in healthy tissues, and phosphoric acid is much diminished; while, on the other hand, the proportion of sodium salts is doubled, and that of chlorine greatly increased.

These proportions derive some importance from the fact that in man, though not in all animals, potassium and phosphoric acid predominate in the corpuscles of the blood and of pus, while sodium and chlorine are the predominant elements of blood-serum. Hence a great loss of pus-corpuscles would produce a deficiency of those elements which are actually found to be deficient, and thus these results confirm the theory of a causal connection between chronic suppuration and lardaceous disease. But as there is not always suppuration, it is evident that this theory is not a complete explanation of the disease.

Amyloid Concretions.—In several parts of the body we meet with small roundish masses of homogeneous substance, sometimes showing a concentric arrangement, like that of grains of starch, which give the same or similar reaction with iodine as do the parts affected with lardaceous degeneration. The reaction with methyl-violet is not constant.

These amyloid bodies are most frequently found in the brain, especially in the ependyma of the ventricles, where they were first discovered by Virchow, and are not necessarily connected with any disease, being found in healthy organs. They also occur in cerebral tumors and in chronic inflammation or sclerotic conditions of the brain and spinal cord. But these formations are not connected with the general or widespread lardaceous degeneration above described; and since accurate chemical analysis is, from the small size of the masses, impossible, it must for the present be regarded as uncertain whether the substance deposited in these situations is the same as that concerned in the more general disease.

Concentric Bodies in the Prostate.—Concretions of concentric structure are often met with in the prostate gland, which sometimes, though not always, give an amyloid reaction with iodine. They are not associated with any disease, and are said by Klebs to be seldom absent in the prostate of elderly persons, while they are also found occasionally in dogs. They are often large enough to be seen with the naked eye, as brownish granules, which were long ago compared to grains of snuff. The general appearance of these bodies on section is like that of a small calculus formed of concentric layers. The process of their formation, traced by Paulizky, appears to be as follows: first, an albuminous deposit is formed in the glandular follicles associated with shedding of the follicular epithelium, and perhaps with degeneration of these elements. The mass thus formed may, by further changes, be so altered as to give a brownish, or, in some instances, a pure blue color with iodine; and by the deposition of successive layers, the stratified appearance is produced. In a later stage, lime-salts, especially in the form of phosphate, are deposited, and the mass becomes a minute calculus. Small calculi of this kind are found in considerable numbers scattered through the prostate, and evidently result from calcification of the concentric bodies. Whether the larger prostatic calculi, polyhedral or facetted bodies sometimes united into considerable masses, are always formed by the same process is a question which cannot here be discussed. At all events, the formation of prostatic concretions is a very different process from lardaceous degeneration.

Fibroid Degeneration.—Though this important change is not, strictly speaking, a degeneration, yet, as the name is often used, it is desirable to explain what is meant by it. In many organs, and in different diseases, we find that the special or parenchymatous elements suffer atrophy or degeneration, while the connective-tissue stroma of the organ is increased. The result is usually that the organ becomes harder and more fibrous, while its special function is impaired or abolished. The ultimate result is that, in place of healthy tissue, we have newly formed fibrous tissue; and the latter being inferior in physiological value to the original, the change is regarded as a degeneration. The term fibrous or fibroid *substitution*, proposed by Dr. Bastian, seems more appropriate, though it is not often used.

According to our definition of inflammation, this process is regarded as chronic interstitial inflammation, but the classification of such changes as inflammatory is not universally admitted. The change receives different names in different organs. When it affects the nerve-centres it is usually called *sclerosis* (which means hardening, though, as a matter as fact, the parts are not hard), and several important diseases are placed under this head. In the liver, fibroid change is called *cirrhosis*, and the same name is sometimes given to the same process in the kidney, otherwise called contracting granular kidney, or chronic interstitial nephritis. Fibroid disease of the lung is a well-recognized morbid condition, though it is with difficulty distinguished from some forms of tubercular disease; and the same change often forms a part of the processes actually set up by tubercle, both in the lungs and other organs. Organs affected by chronic venous congestion causing the changes formerly described (*see* p. 34) are also called fibroid. Moreover, the same change occurs in some organs when they undergo spontaneous or physiological wasting, such as the thyroid gland; and possibly the same is true of the change of the supra-renals in Addison's disease. It is seen also in the walls of the heart, when hypertrophied; and sometimes in the outer coats of arteries.

Variations in the Fibroid Process.—In all these cases there is increase of fibrous tissue; the chief differences consist in the greater or less vascularity of the tissue thus formed. When the tissue is vascular, as in cirrhosis of the liver, there is a great abundance of leucocytes or nuclei in the early stage, and much fibrous tissue is formed. Such tissue is especially liable to contraction, like a scar, and may thus produce, by compression and distortion, secondary changes in the organs. Where the new tissue is less vascular (as in sclerosis of the nerve-centres) there are fewer cells in the early stage and less new tissue is formed. The new tissue, moreover, preserves the properties of the original neuroglia in not being hard. In all cases equally, the parenchymatous tissue, nervous or glandular, wastes and disappears. According to some pathologists, the process in the first case is one of inflammation, in the latter not. Both are here considered as being inflammatory, though the mode of production is different. But the important thing for the student is not so much to know by what name they should be called, as to understand the real nature of the changes in question, and especially the fundamental point of the relation of the atrophic and hypertrophic changes which make up the process which is known as fibroid degeneration.

Relations of Atrophy and Overgrowth.—Now there are three possible relations between these two parts of the process, or, in other words, three hypotheses are possible respecting these relations; either (1) that the connective-tissue increase is the primary change, and causes, by pressure, atrophy of the special parenchymatous elements, or (2) that both are concurrent effects of the same injury, producing, as before explained, simple destruction of the special elements, with hyperplastic inflammation of the connective tissue, or (3) the atrophy of the special elements may cause plastic inflammation or increase of the connective tissue. It is often assumed that the first is the only possible explanation; but we shall have occasion to see that each of these may be true, and that some kinds of fibroid change are to be explained in one way, some in another.

1. The first is assumed to be the regular sequence of events, for instance, in cirrhosis of the liver. The alcoholic poison is supposed to act directly on the connective tissue, which becomes increased and destroys the liver cells by pressure. It is quite possible that this is so, though positive proof is wanting; as it may equally be the case that alcohol poisons and destroys the liver cells directly. The same explanation is generally adopted in the case of the granular kidney, which is thought to be a change starting with the vessels and connective tissue. There is also a disease of the spinal cord, known as focal sclerosis or sclerotic myelitis, consisting of overgrowth of the connective tissue and atrophy of nervous elements, at certain definite spots (not to be confounded with disseminated sclerosis). Here the distribution of the disease corresponds to that of the vessels, not of the nervous tracts, so that there is no difficulty in supposing that the connective-tissue overgrowth is the primary change, and the cause of the other lesions. In all the morbid processes above described, it is clear that the fibroid change is essentially a chronic inflammation.

In induration following venous congestion, it is clear that the process begins with the vessels, and next affects the connective tissue.

2. The connective-tissue growth and wasting of other elements may be concurrent effects of the same poison or injury. This appears to be the case in the changes of the kidney produced by lead, elsewhere described, which begin with parenchymatous degeneration and end with cirrhotic or sclerotic induration. It is probably in the same way that we must explain the change called fibroid of the muscular substance of the heart—at least in some cases. When the rheumatic poison affects the heart the first result, as seen when death occurs during the acute disease, is chiefly rapid degeneration of the muscular fibres; but a later result, or one caused by chronic disease, is increase of the connective tissue leading to fibroid induration. When the fibroid change accompanies hypertrophy without evident inflammation the process is not so easily explained, and no complete explanation has been given, but the appearances are quite consistent with chronic inflammation produced by pressure. That is to say, excessive tension acts upon the muscular substance so as to produce hypertrophy, and upon the fibrous tissue so as to produce overgrowth, just as in the case of external pressure on the skin.

3. The parenchymatous degeneration precedes the increase of con-

nective-tissue. This is probably often the case, but the most convincing instances of the process are to be found in chronic diseases of the nerve-centres, especially of the spinal cord. In what are called the "system-diseases" of the cord, the morbid change is limited to certain nervous tracts. Let us take as an instance the motor tract passing from the motor centres in the brain to the gray matter of the cord, and thence to the muscles. If this tract be completely interrupted at any point, so that the nerve-fibres are cut off from their central connections, they undergo (as stated above) degeneration ending in atrophy. This is the case both in the nerves and in the conducting fibres of the cord forming the lateral columns, etc. The same change in the conducting fibres may occur without any obvious lesion of the central connections, so that it appears spontaneous or idiopathic. Accompanying this nerve-degeneration there is generally, in a greater or less degree, overgrowth of the connective tissue around or among the nerve-fibres. In the conducting tracts of the cord this is a diffuse change called sclerosis. In peripheral nerves it appears as an increase of the nerve-sheaths (perineurium or endoneurium), and is somewhat inconsistently regarded as an inflammation, and called by a different name, such as *perineuritis*.

By histological examination alone it would be difficult to say which of the two changes comes first. But clinical evidence, which here is much more important, proves beyond a doubt that, in some cases at least, the degeneration of the nerve-fibres is the primary, and the connective-tissue growth a secondary change. For instance, in the so-called secondary degenerations, where the conductive tracts are affected by destruction of the ganglionic tissue with which they are connected, it is clear that a break of communication can only at first affect these fibres, and cannot cause any direct injury to the connective-tissue. We are therefore justified in saying that the connective-tissue changes are consecutive to the nerve-changes, and in fact caused by them. By analogy it may be inferred that the sequence is the same in the so-called idiopathic forms of sclerosis, *i. e.*, lateral sclerosis, posterior sclerosis (tabes dorsalis), and others. But it is not necessary to go into this question, because the one instance is enough to prove our point.

If we ask, How does atrophy of the nerve-fibres cause increase of connective-tissue? we enter on a difficult question. But it should first be remembered that, as pointed out before, all elements of the body are so closely packed that removal of one part lessens the resistance pressing on the other, and hence favors overgrowth of those which remain. The influence of this cause may or may not be considerable. But, in the second place, the nerve-fibres in the case supposed are essentially dead; and a dead part in the tissue produces the effect of a foreign body, that is, it sets up inflammation in the parts around. The inflamed zone round a gangrenous mass, the fibrous tissue growth round an embolic block, or a necrotic mass of tubercle, and many other instances, will occur to the memory. From another point of view, we may say that the tissues deal with dead matter as with a foreign body; they form fibrous tissue around it and encapsulate it. In this way does the connective-tissue appear to deal with the dead nerve-fibres; it tends to form a barrier of fibrous tissue around them. At the same time the fibrous tissue may also have an absorbent function; and be, as some think, the means of gradually removing the necrotic parts (see p. 143).

If in this case it is proved that degeneration of parenchymatous elements leads to sclerosis or fibrous hyperplasia, it is clear that this may possibly be the process in other cases where the proof is not complete. For instance, it may explain the fibroid degeneration of organs which undergo spontaneous wasting, such as the thyroid and supra-renals, and may in some cases explain cirrhotic changes in the kidney.

It is not necessary to pursue the subject further; it will be enough to have shown that wasting of parenchymatous elements may be a cause, and not merely a consequence, of connective-tissue overgrowth. Whether this overgrowth is to be called inflammation or simple hyperplasia, is a question of secondary importance. This does not, however, exclude the possibility that the overgrowth thus set up may, as often happens, become excessive, and thus become, in its turn, a cause of injury by pressure to the parenchymatous elements.

Summary of Fibroid Degeneration.—Fibroid degeneration consists essentially in the replacement of the normal tissue of an organ, wholly or partially, by fibrous tissue, and is thus more correctly called a substitution. It is only a degeneration, inasmuch as the new tissue is considered inferior to the original. It consists of a combination of two processes—increase of connective tissue, and wasting of the special or parenchymatous elements. Either of these processes may precede and cause the other, or they may be concurrent. In the chronic diseases called by this name, the two changes do actually proceed simultaneously, although one of them may have preceded and caused the other.

CHAPTER XVI.

HYPERTROPHY.

THIS word, which properly means over-feeding or over-nourishment, is used to signify overgrowth either of the whole body or of a part. Since overgrowth is generally shown by enlargement, an enlarged body or organ is sometimes loosely said to be hypertrophied. But it is important to distinguish true overgrowth from enlargement, which may be due to some additional substance deposited, or to increase of one constituent only of the part affected or to mere dilatation.

Thus, fat deposited in organs may produce a false appearance of hypertrophy, while the organ is really wasted. This is seen in fatty liver and in the condition called pseudo-hypertrophic paralysis of the muscles, when fat accumulates between the muscular fibres (Duchenne's paralysis). Similarly, great corpulence, such as that of overfed animals, is not a true hypertrophy of the whole body, since it affects one tissue, the adipose, only. Any organ may appear to be enormously enlarged by the growth of a tumor, a cancer, or a hydatid cyst within it, when the organ is really wasted.

Hollow organs appear hypertrophied when they are dilated, as the brain in hydrocephalus, when, in spite of the great apparent size, the brain-substance is much attenuated. A dilated heart may have very thin walls, though it appear large, and the excessive distention of the lungs called emphysema is sometimes accompanied by actual wasting of the lung-tissue.

Hypertrophy may be *general,* affecting the whole body, or *local,* affecting one limb, one organ, or one tissue.

General hypertrophy is a remarkable physiological phenomenon, but of little practical importance. It is seen in the production of the abnormal individuals called *giants.*

Giants are usually born of parents of normal size, and very rarely more than one such individual occurs in a family. They are usually of weak constitution, of intellectual capacity below the average, wanting in energy, and possessing feeble reproductive powers. Perhaps for the latter cause the condition is in its most conspicuous forms not hereditary.

Little can be said of the causes which produce giants. Since the tendency to overgrowth begins in early life it would appear to be due to some unknown developmental stimulus, like those which give rise to sports and varieties. Nutrition appears to have little or nothing to do with it. The only notable fact is that giants generally appear among races of men where tall individuals are common. But a relatively gigantic individual might appear among a very small race who would be regarded as gigantic if measured by the average stature of mankind.

The name *macrosomatia* is given to a condition of general enlargement of the whole body different from that of giants in affecting all dimensions equally. It has been observed to be congenital or to come on in early life.

Partial or Local Hypertrophy.—This occurs in two forms, either as (1) *Hypertrophy of Development;* or (2) *Acquired Hypertrophy.* Development hypertrophy is an excessive increase in size of any part of the body, taking place during the period of natural growth, either in intra-uterine or extra-uterine life. This increase begins, in most cases at least, soon after birth if not in the fœtal state, and hence may generally be called congenital; but there are cases of similar abnormal development occurring in adult life when growth is at an end. When such increase begins, the affected part will grow till it reaches a size far beyond the normal as measured by the corresponding part on the other side of the body. The change has been seen to affect the whole of one side of the body, constituting the condition called hemi-hypertrophy, of which several instances have been recorded. In theory it might seem difficult to distinguish this from the condition of *hemiatrophy,* in which the smaller side of the body is the abnormal one, since in either case inequality of the two sides of the body is the main feature. But, generally speaking, either some evidence of morbid wasting on the smaller side or some over-vascularity and increase of temperature on the larger side, will be present to show that in the former case atrophy, in the latter hypertrophy, has produced the inequality. Hemi-hypertrophy is, however, much rarer than hemi-atrophy. In some cases the two limbs of one side have taken on a giant growth. In others one limb only has been affected, especially the leg, and in other cases one side of the head, when the tongue, the hair, and all tissues participate in the enlargement. Sometimes certain fingers are hypertrophied, either on one side only, or (as in Curling's case) some fingers of each hand almost symmetrically.

Parts thus hypertrophied are fuller of blood than normal parts, and have a higher temperature. The cause of such overgrowth is, however, quite unexplained, though it may plausibly be supposed that the original starting-point of the change is in the nervous system.

Acquired Hypertrophies, occurring in the adult body, may be generally referred to some definite cause; but there is a certain class which must be called physiological, as not resulting from any disease or injurious influence.

Physiological hypertrophy is displayed in the most typical form in the enlargement of the uterus which follows impregnation. Here simultaneously with the growth of the fertilized ovum, an enlargement of all parts of the organ occurs, which, though it is accompanied by an increased determination of blood to the part, cannot be regarded as caused by that alone, but must be the result of a definite physiological stimulus. The overgrowth begins with the mucous membrane, which becomes thicker and more vascular; it extends to the glands, the muscular walls, bloodvessels, and every part of the organ, which reaches a weight twenty-four times that of the unimpregnated uterus. It might be thought that the weight of the fœtus, acting mechanically, has a tendency to cause muscular hypertrophy of the uterine walls (in a manner to be presently explained); but that this cannot be the true explanation is shown by the remarkable fact that the muscular uterine tumors, composed of the same tissue as the uterus, also become enlarged during pregnancy, and perhaps diminish again with the involution of the organ.

Enlargement of the mammæ arises in the same manner from what may be called physiological stimulus, connected with uterine development; and some cases of a spontaneous enlargement of the thyroid have probably an obscure connection with the development of the sexual organs.

Enlargement of the prostate in old men is also, so far as we can see, a spontaneous hypertrophy, which, though it is the cause of disease, cannot be referred to any morbid influence.

Other forms of acquired hypertrophy may be traced to the following causes:

a. Increased supplies of nourishment.
b. Increased functional activity.
c. Pressure.
d. Inflammation.

a. **Increased Supplies of Nourishment.**—To supply more food, that is, more blood to any part of the body, does not necessarily cause overgrowth of that part. A clear instance of this law is seen in the results of experimental hyperæmia, such as is produced by vaso-motor paralysis. In the very numerous experiments, for instance, on section of the cervical sympathetic, overgrowth is not generally observed, though there has been, in some instances, enlargement of the bones, muscles, etc., of the part. The few pathological cases of a similar lesion in man have shown, so far as I am aware, in no case hypertrophy. The absence of growth may partly be explained by the fact that experimental hyperæmia thus produced is not permanent, lasting, as a rule, only from fifteen to twenty days, even when the destruction of the nerve is complete. In those cases in which hypertrophy has been observed, the subjects appear to have been chiefly young and growing animals.

In man, also, paralytic hyperæmia may exist for a long time without producing hypertrophy, as is seen in the flushing of the face produced by gastric or uterine derangements, which does not necessarily lead to thickening of the skin. But if there be an addition, some inflammation or excessive activity of the glands, there may result great overgrowth of the tissues of the nose and cheeks, producing the excessive development of some forms of *acne rosacea.*

The most distinct instance of overgrowth from pure hyperæmia is seen in the formation of the corpus luteum of pregnancy, as distinguished from the ordinary menstrual scar. The scar left by the escape of an ovum from the ovary is the same whether the ovum be subsequently impregnated or not. But if it be impregnated there is an excessive afflux of blood to the uterus and its appendages; and this it would seem to be which determines the production of the complicated structure called the true corpus luteum. The same structure has been seen in rare cases without pregnancy, when there has been some special determination of blood to the sexual organs.

b. **Increased functional activity** is the most potent cause of hypertrophy in all organs which have an active function, as is very obvious in the voluntary muscles. In order that this should be the case, the exercise must be vigorous, but not excessive, and not too long continued without rest; and, above all, the general nutrition of the body must be good. A starved man who exercises his muscles will only cause them to waste more rapidly.

The explanation of this process is not quite clear; but it would seem to depend essentially upon the more abundant supply of blood to working muscles, and especially to those working at high tension. The food material supplied by the blood is then, it must be supposed, not quite all used up in the production of mechanical force, but a small surplus is left over for nutrition.

The original stimulus in voluntary muscles is then the nerve-current which produces contraction. The case of the heart is the same as that of a voluntary muscle if we assume the existence of a stimulus producing contraction of variable intensity.

The heart undergoes hypertrophy whenever it is made to work for a long time at higher tension than the normal. It works at higher tension whenever there is increased resistance to the flow of blood through the arteries, either from obstruction at the orifices of the heart (stenosis of the valves), or changes in the arteries, such as rigidity and contraction of the muscular coats; or from any physical condition which alters the relation of the blood to the capillaries, and thus increases friction in these vessels. As a consequence of these conditions it is found that each individual contraction of the heart is more powerful, and the organ passes into the condition of a voluntary muscle which is forcibly exercised.

It is not perfectly clear how the higher tension causes a more powerful contraction of the heart, but two causes will evidently come into play.

Fluid pressure on the inner surface of the ventricles is one of the causes producing contraction of those cavities. (The heart will beat when it is empty, but feebly.) Therefore, the higher the internal pressure the more powerful the contraction. Moreover, higher tension in the aorta must cause a more copious flow of blood into the coronary arteries. For even supposing that there were in these (what is not certain) a high degree of tone, it would not counterbalance the relatively high pressure which is constantly present in the first part of the aorta.

Again, after the closure of the aortic valves, the pressure in the aorta is in such cases still very high; consequently the flow into the coronary arteries will be kept up during diastole. The result of these arrangements is that the heart will receive more blood, and be better nourished when the arterial tension is high. The two factors, increased work and abundant nourishment, being combined, we see how the heart, when the resistance is increased, is in the same case as a voluntary muscle forcibly exercised, and thus undergoes hypertrophy.

Hypertrophy of the left ventricle of the heart is also generally met with in cases of chronic kidney-disease, though in what way it is produced is still a matter of dispute. The probability is, however, that it is caused by the thickening of the muscular coats of the arteries which accompanies the kidney disease, this being both a cause and consequence of increased arterial tension (*see* Chapter VIII.).

Hypertrophy of the right ventricle occurs when there is undue resistance to the passage of blood through the lungs, under the same conditions as on the left side.

Hypertrophy of smooth or involuntary muscular fibre also takes place whenever that tissue contracts under higher tension than normal. This is very obvious in the case of the bladder. When there is any obstacle to the passage of urine, and consequently it is discharged under great pressure, the walls become much thickened. In the same way, the walls of the stomach, the œsophagus, and the intestines may become hypertrophied above any point where there is obstruction. The muscular walls of the arteries, especially the smaller ones, are very liable to hypertrophy; which appears to be connected with a chronic condition of high arterial blood-pressure, but the precise sequence of events producing it is not yet clear.

Arterio-cardiac Hypertrophy.—The most probable explanation is, however, as follows: When high blood-pressure is caused, even transitorily, by some functional variation—it may be a change in the composition of the blood, produced by excessive food or deficient excretion; it may be a disturbance of the nerve-centres—the muscular walls of the whole arterial system (including the wall of the left ventricle of the heart) are subjected to increased strain. If this strain be often repeated or become continuous, the muscular structures become hypertrophied. But this hypertrophy, when once established, is itself a cause of heightened blood-pressure, especially through the relation of opposition, formerly pointed out, between the contraction of the smaller arteries and the heart. Hence the high blood-pressure and the accompanying hypertrophy tend to perpetuate themselves.

The most frequent cause of this arterio-cardiac hypertrophy is no doubt disease of the kidneys, as mentioned above; but it may arise without kidney disease, and may possibly, as some think, be a cause of the morbid changes in that organ.

Glandular organs may, but do not so constantly become hypertrophied from increased use. When one kidney is extirpated or destroyed, the other undergoes hypertrophy, having to do double work. In diabetes, the kidneys are generally enlarged.

There is no real evidence that nervous structures undergo hypertrophy in consequence of increased work, though it has been supposed that the brain increases in size through mental activity.

c. **Hypertrophy from Pressure** or friction obviously occurs only in organs whose functions are passive, such as the skin and the serous covering of the viscera. The pressure must be intermittent and not excessive, since continuous or excessive pressure tends rather to produce atrophy or necrosis, by obstructing the circulation. Instances are—thickening of the skin where pressed upon, and the production of white patches (milk spots) on the pericardial covering of the heart at the spots where friction occurs.

d. **Inflammation**, when long continued, often causes the enlargement of various organs and parts, and may thus be regarded as a cause of hypertrophy; but it generally, if not always, affects one tissue especially, viz., the connective tissue. Thus we have thickening of the pleura, pericardium, dura mater, etc., from chronic or repeated inflammation; and thickening of the skin from chronic eczema. Inflammation of the periosteum may produce permanent enlargement of a bone. In general, acute inflammations do not cause hypertrophy.

Process of Hypertrophy.—Enlargement of an organ may be conceived of as taking place either by the increase in some of the existing cells and other elements, or by the addition of new ones. There can be no doubt that the latter process is the most powerful factor in hypertrophy; but increase in the size of the elements also often occurs. Thus in the pregnant uterus, muscle fibres have been found seven to eleven times the normal length, and from twice to seven times the normal width. In hypertrophy of the heart the primitive muscular bundles are found to be enlarged. In hypertrophy of connective tissue the fibres are usually much thicker than normal. In a kidney which has become enlarged in consequence of the loss of its fellow, the tubules and Malpighian bodies are found increased in size.

Hyperplasia or Numerical Hypertrophy.—Increase in number of the tissue elements is therefore always present in, and is the chief cause of hypertrophy. This process is called *hyperplasia*. It has an importance which goes beyond its mere relations to hypertrophy, since it is a part of the process of inflammation and also the first stage in the formation of many tumors or new-growths. Hence hyperplasia does not necessarily lead to hypertrophy strictly so-called.

CHAPTER XVII.

LAWS OF NEW GROWTH IN GENERAL.

By new-growth we understand the formation of new cells or other elements, by which is effected either the replacement of lost parts or elements of the body, or else the production of a new part.

It is by the formation of new cells that all parts of the body are built up during the process of normal growth, from the segmentation of the impregnated ovum till the formation of the perfect individual; but with normal growth we are not here concerned except so far as it illustrates pathological processes.

All growth starts from the *cell.* By a cell we understand a mass of living protoplasm with one nucleus or more, which may, in some cases, by softening of portions of its substance, by the absorption of other material or by the hardening of its external parts, become a hollow structure, more resembling a vegetable cell, and corresponding to the etymology of the word (from the "cells" of a honeycomb).

Increase in number of cells takes place essentially only in one way, viz., by division of the original cell-mass into two; but, in consequence of variations in this process, it receives under different circumstances different names.

Another method, that of *endogenous gemmation*, in which young cells are formed in the interior of a mother-cell, has also been described; but the interpretation of the appearances thus explained is not free from ambiguity.

Division of the nucleus generally, if not always, precedes division of the protoplasm.

The nucleus appears in some cases to divide by simple cleavage, which is followed by division of the protoplasm. In consequence, we may sometimes see cells with two nuclei pressed closely together, or two cells formed by the division of one, having their nuclei attached to the adjacent surfaces, which show where the division of cell and nucleus has taken place (*see* Fig. 15), and other forms which seem to show that nucleus and cell have divided in the same manner.

Indirect Division.—The latter method, termed *direct division* of the nucleus, was till lately thought to be the only method. In embryonic cells, examined in the living state, and in some forms of cells in the adult organism, however, the division of the nucleus is found to be a much more complicated process which is called indirect division or karyokinesis (movement of the nucleus), because certain movements in the components of the nucleus precede its division. The process is a rapid one, *i. e.*, it occurs in times measured by minutes or even seconds. It can therefore only be traced in living tissues or in those just removed from the living body. It does not appear to be immediately arrested by somatic death; hence in ordinary post-mortem examination of tissues the process will have run its course and come to its natural termination. We do not, therefore, in this case see the process, but only the final result of the process. Its *stages* may be seen in tissues just removed from the living body, by hardening as quickly as possible, and staining by special methods.

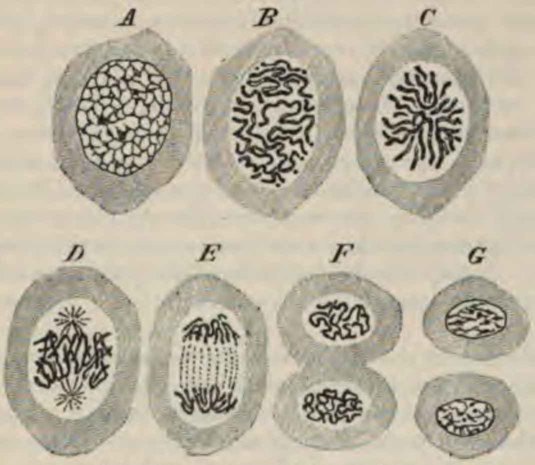
Thus it is possible that the appearances regarded as indicating direct division may really be the *results* of the indirect method; and some have argued that the division of nuclei always takes place by the indirect method. This conclusion is not demonstrated, but cannot be disproved, since direct division of the nucleus has never been positively observed in the living cell.

While division of the nucleus is probably always the first visible step in cell-division, there are doubtless changes in the protoplasm which accompany or possibly even precede it; but these are less known than the changes of the nucleus.

Division of the nucleus is not always followed immediately by division of the protoplasm; hence we may have cells containing two or several nuclei. The latter are called myeloid or giant cells.

The process of production of new cells is called *cell-multiplication* or *cell-proliferation*, the latter term, though of doubtful etymology, being that most commonly used.

FIG. 35.



Karyokinetic figures (after FLEMMING).

A, resting-form of nucleus; *B*, coil-form; *C*, star-form (Aster); *D*, polar division, with formation of equatorial plate; *E*, star-form of daughter-nuclei; *F*, coil-form of the same; *G*, resting-form of the same, with complete division of cell.

It was at one time thought that cells were produced in an amorphous material, or blastema, by "free cell-formation," but of this there is no evidence. So far as is known, all new cells in the body are formed from preëxistent cells, a law which has been formulated by Virchow in the phrase *omnis cellula e cellulâ*.

Karyokinesis or Karyomitosis.[1]—The changes successively observed in the nucleus when a cell is dividing by this process are seen in Fig. 35.

The nucleus of a cell, which was formerly regarded as a very simple structure, has by recent researches been shown to be very complex, being composed of a limiting membrane and contents. The latter, again, is found to be made of two substances—an apparently homogeneous basis substance called the nuclear juice, and a denser, more highly refracting material, consisting of corpuscles or nucleoli and threads. The nucleoli are visible without any preparation; the threads are best seen when stained with some coloring matter such as carmine or, still better, aniline dyes. The nuclear juice does not take any dye. The threads are usually arranged in a sort of network, which, when *at rest*, has the appearance shown in *A*. When the nucleus is about to divide, the first step, according to Flemming, is that the membrane and the nucleoli disappear, while the threads become more distinct, and show rapid movement. They then take the form of a *coil* or wreath (*B*), which may vary in arrangement, but usually takes the shape of loops with their convexity outward, while the centre of the nucleus is less thickly covered. The next form is one in which there is a concentration of threads toward the middle, while their free extremities are directed outward so as to form open loops. This is the *star*-form or *aster* (*C*). The threads then split up, forming a star with finer rays, and then begins a process of polarization. The stars begin to withdraw toward the two ends of the nucleus, while a sort of transverse partition, *equatorial plate*, is formed across the middle. *D* shows this process beginning. In *E* we have the polarization further developed, with commencing division. The two separate coils are beginning to form two daughter-nuclei, and are only connected by faint threads. In the next stage (*F*) two distinct daughter-nuclei, showing the *coil*-form (like *B*) are completely separated by protoplasm, which shows commencing constriction. In *G* the division of the cell is complete, the daughter-nuclei having assumed the resting state (like *A*) and each being surrounded by a membrane.

The transformation above described shows some variations, but processes the same, or essentially similar, have been observed in many normal structures, both animal and vegetable, and in pathological states: for instance, in the embryonal vesicle of certain seeds, *e. g.*, of the fir; also in fertilized ova of insects and other animals; in the regeneration of tissues, such as the cornea after injury, in normal skin, and, probably also normally, in lymph-glands. They have also been traced in various pathological structures, *e. g.*, in rapidly growing sarcoma and carcinoma, in cancerous lymphatic glands, in condylomata, in the formation of callus from periosteum, in endothelial cells of bloodvessels during the organization of a thrombus, in the medulla of bone from certain cases of anæmia, and in early stages of the formation of tubercle after inoculation. It is possible that in some of these cases the appearances were really normal, and not produced by the disease affecting the organ examined; but they always indicate cell-proliferation, of which the karyokinetic figures, when observed, are important and undeniable evidence. The complete sequence of figures given above (much abridged) from Flemming was observed by him in living tissues. When dead tissues, normal or morbid, are examined, the different stages of karyokinesis are of course only seen, if at all, in isolated cells; and the succession could only be traced by putting together a number of observations. The appearance of a lymph-gland, with karyokinetic figures, is seen in Fig. 36, but in ordinary pathological formation they are less abundant than here.

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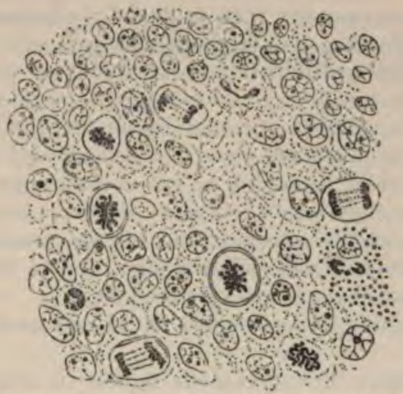
[1] Karyokinesis is from the Greek *κάρυον*, nucleus or kernal, and *κίνησις*, movement. Karyomitosis means nucleus-weaving, the latter part of the word being derived from the Greek *μιτόω*, I weave.

FIG. 36.



Karyokinetic figures in nuclei of lymphatic gland (after FLEMMING).

Occurrence of Cell-proliferation.—Cell-proliferation occurs physiologically in: (1) The formation of all tissues from the ovum, in embryonic and post-embryonic life.

2. Processes of evolution which occur in the progress of the organism from youth to age; for instance, ossification, and the changes which result in the production of fibrous tissue in various parts, such as the omentum, which becomes more fibrous with advancing age; and the same process probably goes on in most serous membranes.

3. The production of new epithelial cells in the normal process of secretion in glands. These are best seen in the mammary gland, the testicle (seminiferous tubes), etc.

4. In lymphatic glands there is a constant production of new lymph-cells, and probably the same takes place in the medulla of bone and perhaps in other parts.

Cell-proliferation occurs pathologically in:

1. The reproduction of elements destroyed by disease or injury. Examples are the restoration of tissue in the neighborhood of wounds; the reproduction of muscular fibres which have undergone degeneration in fevers, etc.

2. In the neighborhood of, or even in the midst of inflamed parts. But here it is doubtful whether these changes are not merely reproductive to replace destroyed elements, or else normal processes which go on with greater intensity than usual (*see* Inflammation).

3. In the production of new-growths or tumors.

Evidence of Cell-proliferation.—It is often an important practical question how this change is to be recognized in microscopic examinations *post-mortem*, since the process cannot be actually watched.

The following appearances generally indicate cell-proliferation.

1. Groups of cells, belonging or not to the normal structure of the part, two or more together, which show by their form that they have been produced under circumstances of mutual pressure (*see* Fig. 15).

In early stages of sarcoma or carcinoma, and in the parts surrounding tubercle, these changes are very evident.

2. Cells containing hypertrophied nuclei, or containing two or more nuclei.

3. The occurrence of karyokinetic figures in tissue-cells. This is one of the most certain proofs of cell-proliferation, though not often available.

4. An abundance of nulcei or small cells indistinguishable from nulcei, in abnormal situations, provided we can exclude the possibility of their being leucocytes, is regarded as evidence of "connective tissue proliferation."

The chief source of fallacy in these observations is that leucocytes, either scattered or in groups, may give the appearance of new cells produced on the spot. Hence it is not safe to speak of cells which have no distinguishing characters as new cells, but only when they show some of the pecularities mentioned under (1) and (2).

Thus the appearance known as "small-celled infiltration" was at one time regarded by Virchow as showing the production of a number of new cells of an embryonic type, out of which various tissues might be formed. But we now find it impossible to distinguish these from leucocytes.

Leucocytes are known to have powers of spontaneous movement; they can "migrate" from bloodvessels to tissues, or *vice versâ*, and in the tissues make their way along connective-tissue spaces and lymphatic capillaries, whenever the plasma penetrates. Such leucocytes are called "migratory cells." They may generally or often be distinguished from the fixed cells by becoming more deeply stained with coloring reagents (as logwood or carmine) than the fixed cells of the part. In this property they resemble nulcei rather than cells. By this test we shall find that "small-celled infiltration" means infiltration of the tissue with leucocytes; and is generally the result of inflammation.

A very important question is, Can migratory leucocytes develop into larger and more complex cells, like tissue-cells and thus form new tissues? This is still undecided as a general question, but has to be considered in special cases.

In the case of new-growths there is no evidence that leucocytes ever undergo this developement. We can generally draw a sharp distinction between migratory cells and the cells of the new-growth. There is no proof that the new-growth proper is formed of leucocytes; though there is often some accompanying inflammation which causes an accumulation of leucocytes around or in the midst of it.

CHAPTER XVIII.

ON TUMORS OR NEW-GROWTHS.

WHEN the human body has reached its full standard of growth there is, as a rule, no addition to it of any new part or organ; and if any distinct part or organ is removed it does not, generally speaking, grow again. To this rule there are very rare exceptions. For instance, it has been known that a congenitally supernumerary finger, when removed, has grown again more than once. But such exceptional cases do not invalidate the general rule, that no growth takes place normally from the adult body. This does not exclude formation of new elements (hyperplasia) for the enlargement of an existing organ, or hypertrophy; nor new formation of certain tissues for the purpose of repairing injuries.

Under certain circumstances, however, new growth takes place from particular tissues of the body and forms a mass, sometimes composed of one, sometimes of more tissues, either in a mature or an immature state, supplied with bloodvessels, and sometimes receiving nerves, from the general vascular and nervous systems respectively.

Such a mass is termed a new-growth or tumor, which words may now be taken as synonymous, though the latter had once a much larger signification, being used for any kind of swelling.

A new-growth is distinguished from a normal organ or part of the body (such as a gland or limb) by the following characters:

1. Its growth is not defined by any obvious limit. It goes on growing, generally speaking, so long as it continues to exist, even though certain portions of it may suffer involution.

2. Its shape is not controlled by any special law of growth, or is not typical, but is irregular, depending upon the resistance met with and the facilities for growing in any particular direction.

The latter character is one of those which distinguish new-growth from hypertrophy; and the same distinction is shown by the fact that

3. The tissue of a new growth, though of the same class as the tissue from which it springs, is never precisely the same.

New-growths are again distinguished from normal parts by having no definite *function*. Even when they are composed of elements which normally have an active function, chemical or mechanical, they are not arranged in such a way that the appropriate chemical or mechanical work can be done. A tumor or bone, for instance, has not the mechanical relations which a normal bone, even when hypertrophied, has; it does not exercise the same mechanical functions. So a tumor may grow from the uterus, composed of the same unstriped muscular fibre as the organ itself, but from the arrangement of its parts it does not exercise the supporting and contracting functions of the uterus.

Again, when a tumor is formed from the mammary gland chiefly composed of elements resembling the glandular secreting cells, these cells may undergo a metabolism, or fatty transformation, analogous to that metabolism by which milk is formed. But from the arrangement of parts there is no true secretion, and no true milk is formed or excreted.

Now, in the case of all organs of the animal body which have an active function, the exercise of the function involves "liberation of energy" and consumption of material, so that a part of the nutrition which they receive is thus used up. But if new-growths which exercise no functions and liberate no energy, are abundantly nourished, the whole of the nutrition can be applied to growth, as is the case with vegetable structures. Thus they may be said to exhibit *vegetative life*; and, since they lose nothing by exercising functions, they continue to grow so long as they are supplied with nourishment. Again, the amount of nutrition (or blood-supply) which such growths attract to themselves, bears no relation to the needs of the organism. It is, relatively, in excess. Thus we see how it comes to pass that tumors have an excessive, or apparently unrestrained, power of growth,

The above characters distinguish the process of tumor-growth from the process of formation of a new limb, and also from the process of hypertrophy of a pre-existing part. They mark out tumors as being something abnormal. There is, however, one other abnormal process in which new elements are produced, and by which masses may be formed having a considerable resemblance to new-growths—namely, inflammation. The question then arises—What is the essential difference between inflammation and tumor growth, and how may their products be distinguished from one another?

Distinction between Inflammation and New-growth.—The first distinction is one of causation. Inflammation is the result of some injury, while new-growth cannot, with rare exceptions, be referred to any such cause. Even if an injury should precede the formation of a new-growth, there is a clear distinction between the two processes, the changes denominated inflammation being always antecedent to the new-growth and usually ended before this begins.

Next, the old definition of inflammation as swelling, accompanied by pain, heat and redness, should be borne in mind. For the latter characters are not necessary accompaniments of new-growths, though they may be present, either in consequence of the hyperæmia consequent on growth, or because the new-growth itself may be the subject of inflammation.

Again, the process of inflammation is essentially the same in all parts, while new-growth is different according to the tissue from which growth takes place.

Inflammation is also essentially destructive in the first instance, though there is a process of reconstruction; while new-growth is essentially constructive, the destruction, if any, being purely mechanical, or consisting only in a substitution of the original tissue by new tissue.

Finally, there is a most important difference in the products of the two processes.

New growths are distinguished from the products of inflammation by

1. The permanence of their structures; while in inflammation the products have only a short life, generally speaking, even the most permanent, *i. e.*, granulations, serving only a temporary purpose.

2. The products of inflammation, if more permanent, reproduce one type of tissue only, viz. connective, while new growths reproduce various types of tissue.

3. The elements of inflammation are emigrated leucocytes, which do not form the essential cell-elements of new growths.

There is a certain class of formations which have been sometimes regarded as new growths, sometimes as the products of inflammation, and sometimes as intermediate between the two. They are known as granulation-tumors, or infective granulomata, and in this work are arranged as the products of a special kind of inflammation resulting from the irritation of a continuously acting poison special to each disease, which poison is in many cases demonstrably, in others probably, connected with a minute vegetable organism.

They are, therefore, not new growths in the sense in which the word is here used.

New Growth in Relation to Embryology.—The growth of the embryo normally proceeds by a manipulation of cells, and the mass of cells thus produced undergoes *segmentation*, so as to become arranged in certain layers, from which the several organs and tissues of the body are derived. Thus the "segmented germ" or *blastoderm*, comes to consist of three layers, called the epiblast, mesoblast, and hypoblast.

Certain parts are developed from each of these. From the *epiblast* are formed the central nervous system, the epidermis, and epidermoid tissues, with certain adjacent portions of mucous membrane, and the epithelium of the sense organs. From the mesoblast arise the connective-tissues, the muscles and bones; from the hypoblast, the epithelium of the alimentary canal, and of the glands formed from it, viz. lungs, liver, pancreas, etc.; while the mass of these glands is formed of mesoblast. According to the most recent researches the same is true of the glands belonging to the genito-urinary tract, as the kidney, testicle, etc.

The great serous cavities—peritoneum, pleura, etc.—are generally regarded as cavities formed in the mesoblast. The layer of cells lining these cavities is called *endothelium*, to distinguish it from the *epithelium* lining hypoblastic cavities. But here, again, recent embryological researches show that the endothelium of serous cavities also originates in the hypoblast, so that the distinction of endothelium and epithelium is one of structure only, not of origin.

The formation of new growths or tumors is a process essentially dependent upon the activity of cells. The cells from which the growth starts, grow, increase, and multiply according to the laws already described.

In this way a mass of new cells is produced, which may either (1) go on to reproduce the original tissue from which it started, so that we have a mass of fibrous, bony, fatty, or other tissue, or (2) it may produce cells like those of the original structure, but arranged in an entirely different way, as when we find cells like those of a gland scattered in irregular masses through the connective-tissue, or (3) it may remain in an imperfect or embryonic condition, that is, a mass of cells resembling those of the embryo.

Tumors resulting from the first process are called simple tissue tumors; those resulting from (2) and (3), carcinoma and sarcoma respectively.

New growths have been broadly distinguished into classes, according as they arise from the tissues formed out of these three embryonic parts respectively, as mesoblastic, epiblastic, or hypoblastic.

Mesoblastic tumors would be those formed from connective-tissue in its various forms—fibrous, fatty, bony, cartilaginous, etc.—and from muscle.

If these growths reproduce one of the normal types of the original tissues, they form the simple histioid tumors.

If the development stops short, so as to produce only an immature form of connective-tissue resembling embryonic tissue, the tumor is called a sarcoma.

Till lately the kidneys, and testes, and ovaries were included among the mesoblastic organs, though they are so different in structure. Growths derived from these organs have, however, more resemblance to those derived from hypoblastic and epiblastic structures than to connective-tissue growths. This is explained, on more recent views, by the fact that the serous cavities, peritoneum and pleura, which were formerly considered as formed in the midst of the mesoblast, are shown to be a development of the hypoblast, and consequently the genito-urinary epithelium, which arises from the primitive peritoneum, will be equally hypoblastic. Growths of a strictly epithelial type arise from these organs; just as their normal epithelium resembles that of secreting glands. Hence growths arising from the genito-urinary organs, which offered an insuperable obstacle to the classification of new-growths on an embryological basis, are now brought under a uniform system of classification.

We shall then arrange new-growths primarily on the basis of a distinction between the mesoblastic, epiblastic, and hypoblastic tissues.

We then get two main divisions of new-growths:

Tissue-growths, including those formed from all kinds of connective-tissue and its derivatives. This includes all mesoblastic tissues.

Epithelial growths—namely, all formed from hypoblastic and epiblastic epithelium, with the glands derived from them; and including those formed from the epithelium of the genito-urinary tract.

Growths of pure nerve-tissue ought, on the ground of development, to find their place among epiblastic growths; but since what are called nervous tumors, generally, if not always, originate in the connective-tissue of the nerve-structure, this distinction need not be considered.

Causes of New-growths.—It is not generally possible to say what causes the tissue-elements to multiply in such a way as to produce a new-growth or tumor.

There is no evidence of the existence of any specific poison, such as those which, by continued irritation, produce the granulation-tumors or infective granulomata. Nevertheless, there is no proof that such a virus does not exist, and in certain cases there would be some plausibility in the hypothesis that a growth is produced by some such cause. This is true of certain kinds of lymphoma or lymphosarcoma. In some cases mechanical injury appears to have some influence in determining the place at which a new-growth appears.

Thus the origin of cancer of the breast has been sometimes traced to a blow or other injury of the part. In others, an injury to the eye or to a bone, has been followed by a developent of a new-growth of the part injured. Instances of this are found in the origin of some sarcomota and enchondromata. The development of the new-growth may follow soon after the injury, or not till long after, when the injury is completely healed; so that it is really a growth from a scar, or in a damaged part. The latter case appears to be the more common.

In another class of cases, a slight injury or irritation long continued appears to promote the production of new growth. Thus epithelial cancer has often been observed to occur on the lower lip, where irritated by long continued friction with a tobacco-pipe; on the tongue, at a point where there is irritation from a broken tooth, and so on. The prolonged contact of soot has been observed (in former years more often than now) to develop skin-cancer in the scrotum of chimney-sweeps. Of late years cancer of the skin has been rather frequently observed in workmen who have to do with the preparation of mineral oils, and has received the name of "Petroleum Cancer." The irritation of the oil produces chronic inflammation of the skin, or eczema, which is in certain cases followed by a growth of epithelioma.

But cases of alleged origin from injury form a small proportion of all cases of new-growth. In certain classes of growths—for instance, medullary cancer, including cases now called sarcoma—it has been placed as high as one-third by Paget, but other authorities give a much smaller proportion. Of hard cancers less than one-sixth were attributed to injury; of simple tumors about one-fifth. Taking all classes of growths together, other statistics give one-seventh (14 per cent.) as attributable to injury, others not more than half that proportion.

It has again been pointed out that the most common seats of certain new-growths, especially cancer, are such parts of the body as are normally exposed to friction and irritation. Thus cancer of the digestive canal occurs at the orifices, where the tissues are exposed to friction and irritation—the mouth, the pylorus, the rectum—much more frequently than intervening parts. So in the uterus, similar growths occur most frequently at the os uteri and cervix, less frequently in the fundus.

It has also been observed that new-growths, especially cancer, occur in organs which have been for a long time affected with chronic inflammation. This, like long-continued irritation, must doubtless be considered a weakening condition. In general, a damaged or weakened state of the tissues is favorable to new-growth.

It appears that some kinds of new-growths are more likely than others to be produced by injury, as will be shown in speaking of the particular kind.

In the meantime one broad generalization may be laid down. Violent disruptive lesions, such as fracture of bone, have often been observed to precede the formation of sarcoma, and also of certain simple tissue-tumors, especially enchondroma; while chronic irritation has not been found to have any connection with the production of such growths. On the other hand, chronic irritation often seems to lead to the production of simple epithelial growths, such as simple warts, or so-called "venereal warts," and to be at all events a frequent antecedent of epithelial cancer. But sudden or violent injuries have not been found to have much to do with the production of the latter class of growths.

There is a great difficulty in supposing that mechanical injury, by itself, or even the long-continued effect of a series of small injuries, which we call irritants, can possibly be the exciting cause of new-growth.

Injury is a cause of death, not of growth; and almost the only way in which it can be conceived of as acting so as to cause tissue-elements to grow, is by drawing more blood to the neighboring cells which are not injured, and thus stimulating their nutrition. It must, in short, be the reaction after injury, and not the injury itself.

It may also be conceived of as possible that injury, by forming a breach of continuity, allows certain cells to grow more freely which were formerly kept in a quiescent state by the pressure of surrounding parts.

But for either of these results to follow, there must be something abnormal, or at least unusual, in the parts affected. We know what the ordinary results of injury and of reaction are; the only new growth which they set up is one of a homogeneous kind, which is generally transitory, and gives place to some kind of normal tissue. But in the case of tumor-growth, we have a heterogeneous or heterologous production, which is permanent and does not give place to normal tissue. What is the cause of this difference?

If we say that a tumor (such as a sarcoma) is an abnormal development of an ordinary scar, the question still remains, why, instead of an ordinary scar, we get a sarcoma.

The question is still more unavoidable and necessary to be asked because tumor-growth after injury, though sufficiently common to have been observed in a definite number of cases, is an extremely rare event. Thousands and tens of thousands of injuries are inflicted which are not followed by any tumor-growth, till at length a case occurs in which a tumor results from an apparently similar injury. In attempting to answer this question, it is of no consequence what proportion of tumors are preceded by injury, or what proportion arise spontaneously, nor is it of any importance to inquire what kind of injury was inflicted. These points are very interesting, but not precisely relevant. If, then, we put it in the simplest way: What was there, in the particular case supposed, which caused the injury to be followed by a tumor? the only answer can be that the tissues injured were not perfectly normal; there must have been something in them which is not in ordinary tissues.

A remarkable instance of this law is seen in the production of cartilaginous tumors from the testicle. These growths have been in several cases distinctly observed to follow an injury to that organ. Now if instead of or besides the inflammation which commonly results from injury, we have a cartilaginous tumor produced, it is plain that the part injured cannot have been really normal. It must have contained what a normal testicle does not contain—some tissue or material capable of growing into cartilage—which material, being injured, has shown a reaction altogether different from the ordinary reaction of testicle-tissue after injury. It seems clear, then, that injury, though it may determine the production of a tumor at any particular place or time, cannot be the cause of new growth in general.

Also it is quite clear that the mere state of health of the tissues cannot be the determining cause. Some tumors arise in cachectic persons or debilitated organs; but a great many take their rise in a condition of perfect health, and very often (especially sarcoma) by preference in young people: so that the true determining cause is still to seek.

But it is well to point out that there need not be, and probably is not, any *one* such stimulus. The actual exciting cause, in each of the great classes of new growths, is probably different. There is no reason why a muscular tumor of the uterus, a sarcoma of bone, and a cancer of the breast should not be produced by the same or even similar causes.

The only point common to all is that there must be some inherent or acquired property in the tissues which causes them when injured, or even without any obvious injury, to grow in this peculiar way.

Hypothesis of Tumor-growth from Embryonic Rudiments.—Considering tumor-formation as a species of growth, not of disease, and considering growth (including under this term development) as a manifestation of the original initial impulse by which the body formed and grew up to the adult state, it seems natural to inquire whether tumor-growth may not be due to some portion of that initial impulse of growth not yet exhausted.

Most parts of the body, and probably in most persons all parts of the body, have exhausted their possibilities of growth, and are no longer capable, under any circumstances, of producing new tissues, except the scar tissue which is common to all parts after injury.

The question is whether there are any parts of the body which still possess the power of growth and development which belonged to all tissues in the embryonic state. In other words, are there any parts of the body which contain embryonic materials still possessing the capability (though perhaps quite latent) of being worked up into new tissues?

The supposition that there are still some such undeveloped or embryonic materials in the body is the basis of the theory of Cohnheim, which, whether true or not, is certainly the only one which, up till now, gives any reasonable explanation of the origin of tumors.

Cohnheim supposes that in an early stage of embryonic development more cells are in some cases produced for the formation of a particular part of the body than are actually used up in its formation. Accordingly a certain quantity of building material—so to speak—that is, a certain number of embryonic cells, remain unemployed. This may be a very small mass but, being embryonic tissue, has great capabilities of growth. It may be supposed to date from a period between the differentation of the three primordial layers and the formation of the rudimentary organs. Such a mass may be composed of one tissue, and distributed through the body wherever that tissue is produced, so that one whole system—for instance the skeleton, may have these embryonic rudiments distributed over it, and thus be capable of exhibiting anomalous growth almost universally. On the other hand, it may be strictly limited to one spot.

Such a rudiment may remain for a long time, or possibly through the whole of life, without further development. On the other hand, it may, at some particular period in the development of the body, or in consequence of some special stimulus, proceed to pass through an evolution similar to that of the embryonic tissue of which it originally formed a part.

These supposed embryonic rudiments would be, in fact, a sort of "animal buds," comparable to the corresponding structures in the vegetable kingdom. The stems of trees and most of the higher plants form a large number of buds, some of which grow into branches, but others remain for an indefinite time in a rudimentary condition, until some change in nutrition or other stimulus causes them to develop. When this takes place the bud may develop into a normal branch or, on the other hand, it may grow into a sort of abortive branch or irregular swelling, which is precisely analogous to a tumor of the animal body.

It is easy to speculate on the possibilities of growth of such rudimentary structures. But it is only necessary to discuss the hyphothesis in its simplest form, namely, that such rudiments exist. It must of necessity be impossible to prove that they exist before they grow up into visible tumors, but certain facts are known which give some support to the theory.

Some years ago Virchow showed that islands of unossified cartilage may exist at the end of the long bones, quite distinct from the permanent articular cartilage, and he supposed that such might be the origin of new-growth or of cartilaginous or bony tumors. Such masses of cartilage may often be seen in bones affected with rickets.

Cartilage is undeveloped bone, and thus these masses precisely correspond to Cohnheim's supposed embryonic rudiments, that development being conceived of as arrested at an earlier stage.

In the formation of what are called teratoid tumors, (described farther on) pathologists have long recognized a process similar to that supposed. For instance, dermoid cysts are clearly produced by pieces of skin pushed or drawn inward at an early period of development, and then covered up or buried by the other tissues. They may remain quiescent, or may go on producing skin-appendages, hairs, sebum, and the like, while increasing greatly in size.

The facts of hereditary predisposition to cancer are adduced by Cohnheim in support of his theory. It is certain that tumors are not directly transmitted from the parent to the ovum like congenital diseases; but still the generally accepted law is that certain families show a predisposition to develop tumors (cancerous or other) in after-life.

A similar law prevails with respect to the transmission of anomalies such as supernumerary fingers, peculiar states of the hair or special properties of tissues, as in hæmophilia. What is inherited is not a disease, but something embryonic, or a property of embryonic tissues.

Further, the fact that many tumors are congenital, and a still larger number occur in early life, suggests that, in those cases, a mass of embryonic tissue existed at birth, capable of development.

In other cases, though the actual tumor is not congenital, it takes its rise in a congenital spot, such as a mole or small wart, which after a time—for some unexplained reason—takes on excessive growth. This is just such a rudimentary germ as Cohnheim's theory supposes in the case of other tumors.

Another remarkable fact connected with tumors is that they arise, with rare exceptions, from tissues of the same kind as themselves, though, it may be, in an earlier or later stage of development. On Cohnheim's view they start, not from the perfectly formed mature tissue of the part, but from a rudiment of embryonic material, which naturally develops into that tissue if it grow at all.

All these and many more facts would receive a simple explanation if this theory were proved to be true.

Objection to Cohnheim's Theory.—It is not enough that a hypothesis should be capable of explaining a series of facts. Before it is accepted as the true explanation, the cause supposed must, in the first place, be proved to exist, and then it must be shown that no other cause would produce the same effects. It is not claimed that the cause assumed by Cohnheim's theory has been proved to exist generally, and therefore, for the present, this theory cannot be accepted as a part of science. But no other explanation has been suggested which accounts for so many facts.

On the whole, it would seem to be much more applicable to tumors occurring in the young, and to sarcoma, than to those occurring in advanced life, and to cancer; and it does not in any way account for the remarkable difference between the mode of growth of simple and malignant tumors respectively.

On the Classification of New-growths.—New-growths have been classified on various principles. First, they may be divided into the *homologous* and *heterologous*.

Homologous are those which are like normal tissues; heterologous, those which are unlike any normal tissue. The first class includes growths composed of fibrous tissue, cartilage, bone, or any variety of the connective tissues, also those composed of muscle, and, further, those which reproduce the type of the normal secreting glands and those composed of normal epidermis.

The second class includes those composed of connective-tissue cells, arranged in a manner different from normal tissues, and also those containing epithelial cells, either pavement, cylindrical, or glandular, but arranged in a manner unlike that of normal surface-epithelium or normal glands.

Now since the elements of new-growths are never fundamentally different from the elements of normal tissues, either in a perfect or in an immature condition, the difference between homologous and heterologous thus comes to be one of arrangement, or, as it is said, of *type*. Hence for these names we might substitute the names *typical* and *atypical*.

The only objection to this division of new-growths is that it is not always precise and is sometimes difficult to apply, because the tissues of the homologous new-growths are not precisely like, though similar to, normal tissues. But, broadly speaking, the distinction is a valid one.

Homoplastic (or homoioplastic) and *heteroplastic* are terms which have been used in a somewhat similar sense. The former means that the new growth is like the structure of the part from which it grows or in which it is found; the latter unlike. For instance, an exostosis or bony growth from bone is evidently homoplastic; but if we should find a bony tumor in the lung it would be heteroplastic, even if like normal bone in structure. All strictly heterologous growths must obviously be heteroplastic. This distinction, first made by Virchow, was once thought to be very important, but further research has diminished its significance for the following reasons:

It has been shown that the great majority of new-growths are in a broad sense homoplastic—that is to say, connective-tissue growths arise from some kind of connective-tissue, epithelial growths from epithelium, and so on, though with differences of arrangement or type. The cases of heteroplastic growth may be regarded as exceptional and usually susceptible of some other explanation, as will be shown hereafter.

But, on the other hand, no growth is strictly homoplastic, since, as has been said, the tumor-growth is never precisely identical with normal tissue. This distinction, then, cannot be used with precision as the basis for classification of tumors.

Innocent and Malignant Tumors.—The most important distinction from a practical point of view, which it has been attempted to draw between different classes of tumors is that which is expressed by saying that they have or have not the properties called malignant.

This distinction was originally made without reference to structure, on the basis of the physiology or life-history of tumors.

The term malignant was used for tumors having the following properties:

1. Recurrent—that is, if removed, liable to recur and sometimes to be followed by the production of other growths of the same kind in other parts of the body.
2. Destroying the part in which they grow.
3. Producing great cachexia or constitutional disturbance.
4. Incurable, or at least very difficult to cure.
5. In consequence of the above properties, fatal, or at least likely to destroy life.

Experience has shown that all these properties are essentially dependent upon the first two, since (3) and (4) are not constant, or exist in very variable degrees; and that they are all, in fact, only ways of starting one capital point in the mode of growth of the tumors called malignant, namely, the following:

Such growths do not remain confined to the tissue in which they originate, but spread to the neighboring tissues either by direct contiguity, or by entering into the lymphatic or blood vascular channels, and may also give off particles, which being transported to distant parts produce growths of the same structure in them. Such growths are called secondary or metastatic.

For instance, we may have a tumor in the mamma, which, however large it becomes, does not grow into the neighboring tissues, but produces only a separable lump. Such a tumor is called simple or innocent; it may be a fibroma, adenoma, or so on.

But there may be a tumor forming a far less considerable mass, but which may grow into the skin and into the subjacent tissues, making them adherent and immovable, and is hence called *locally infective*. Next it may pass into the axillary glands, producing tumors there like the original; and, finally, it may give rise to secondary growths in distant parts, such as bone, liver, brain, etc. It may, that is to say, be *generally infective*.

Such a tumor is at once recognized as malignant, and is called mammary cancer. In the same way a growth of the epidermis may, instead of forming a mere projection on the surface, burrow downward into the corium and connective tissue, producing a series of phenomena like those just described. This, then, is malignant, and is called epithelioma.

It should also be noticed that this infective property is seen at a very early period of the growth of such tumors, and is therefore not an acquired property.

The infectiveness of malignant tumors has a remarkable parallel in inflammation (especially suppuration and specific inflammations).

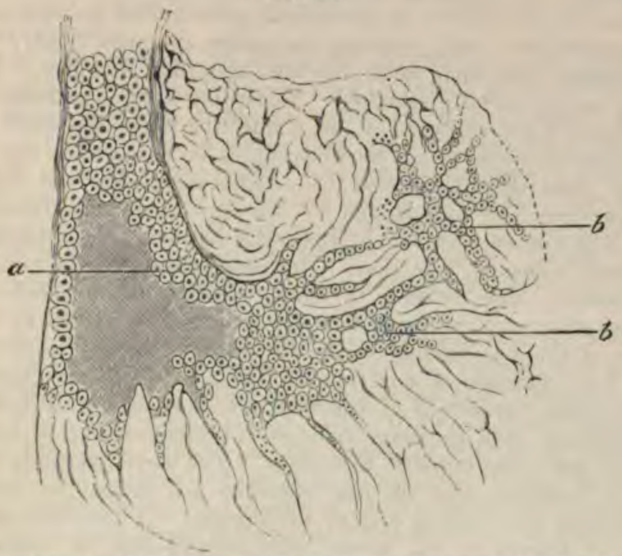
For instance, pus from a crushed bone may burrow into the surrounding parts, and in cases of pyæmia give rise to secondary foci of suppuration in distant parts. Compare also the production of a primary syphilitic lesion at one part of the body; and the occurrence of secondary syphilitic inflammations in other organs.

The analogy between the process of malignant tumor-growth and that of specific or infective inflammation has naturally led to the supposition that some specific poison may be the cause of the former as it is of the latter. It would be rash to say that such a mode of causation is impossible, but at present no such poison has been found to exist in the case of malignant tumors, and little or no evidence has been given pointing to the probability of the existence of any such virus.

Local and General Infectiveness.—The two properties above referred to by this name require further elucidation.

Local infectiveness is best seen in malignant epithelial tumors called cancers, though the property does belong in a less degree to malignant tumors of the connective-tissue class called sarcoma. What is meant by it may be seen in Fig. 37.

Fig. 37.



An acinus of mammary gland, showing growth of cancer and infiltration of connective-tissue (after Waldeyer).

a, cavity of acinus with proliferation of glandular epithelium: *b*, columns of new cells spreading through the connective-tissue spaces.

Here is shown a terminal acinus of the mammary gland, where the epithelium, instead of being arranged in the usual manner on the basement-membrane, is greatly increased or proliferated, altered in form, and scattered in a disorderly manner through the lumen of the acinus. Further, it will be observed that the basement-membrane of the acinus at its blind extremity has entirely disappeared, and the cavity is continuous, by means of several prolongations, with the spaces of the surrounding connective tissue. Into these spaces the cell growth penetrates, and it will be seen that the further the cells are moved from the original glandular acinus, the smaller and rounder they are.

What appears to have happened then is: (1) Abundant proliferation of the glandular epithelium, producing cells smaller and rounder than normal; (2) destruction of the limiting basement-membrane; (3) passage of somewhat altered epithelial cells into the connective-tissue spaces. On these three cardinal points the whole history of malignant growth depends.

1. The new elements resulting from cell-proliferation are not only more embryonic in their character than the original cells, but have been seen to show amœboid changes and movements like those of leucocytes. Hence they will possess some power of migration through the tissues. We suppose, then, that the cells in the connective-tissue spaces at *b b* are derived by continuous growth from the original glandular epithelium; and insinuate themselves the more readily into the tissue spaces from their small size and abnormal mobility. But this view is not universally accepted. According to some pathologists, the outlying cells are elements of the connective tissue modified so as to become cancer-cells. This modification is supposed to be caused by a specific virus spreading from the original cancer-cells to the tissue-cells—a view first propounded by Virchow more than twenty years ago. The influence of the original cells has also been represented as a *seminal* influence, like that of the sperm cell or the germ cell in fecundation. The validity of these explanations depends entirely upon whether, as a matter of fact, the growth does extend by the conversion of the neighboring connective-tissue cells into cancer-cells or not. This question is not conclusively settled. Some pathologists still hold that tissue cells of various kinds may be so modified by the neighborhood of a growing tumor as to become converted into, or to produce, cells like those of the tumor. The more generally accepted view is, however, that all new elements are formed by continuous growth from the existing cells of the tumor; and that the connective tissue, if altered at all, shows only hyperplastic or inflammatory changes. The appearances will, no doubt, often bear either interpretation, but, as an expression of individual judgment may be expected, I must say that, after examining many primary and secondary cancers, I believe that all the cells of such tumors are formed by continuous development from those originally affected; and that there is no such thing as conversion of the elements of the connective or other surrounding tissues into cancer-cells.

2. The second point is the destruction of the basement-membrane, which permits cellular infiltration of the surrounding tissues. Precisely how this is caused, we do not know; but it would appear to be

something more than the mere mechanical effect of pressure. The growing cancer-cells appear to have a power of softening or dissolving the tissues, so as to facilitate their own passage through them. This power may be presumed to depend upon some ferment substance produced by them, though no such substance is known. The supposition is, however, supported by the fact that most cancers—by which class of growths this infiltrating power is chiefly shown—are derived from the epithelium of secreting glands. Owing to this power of lessening the resistance of the surrounding tissues malignant growths are able to pass through the natural boundaries of organs, and affect neighboring parts by direct continuity. This is most strikingly seen in certain malignant lymphatic tumors which originate in the mediastinum, probably in the lymphatic glands, and soak through into the lungs, the pericardium, and even into the heart itself. It is also seen in abdominal cancers when they leave the organs in which they originate, and pass, for instance, into the vertebral column. Many other similar instances might be quoted.

3. The considerations above mentioned sufficiently explain the third cardinal point, namely, the penetration of tissues by the cells of malignant growths.

General Infectiveness of Malignant Growths.—The property of *generalization*, or becoming transmitted to distant parts, which malignant tumors possess, is really an extension of the property of *local* infectiveness; in virtue of which they grow into the lymphatics and bloodvessels and thus pass along the ordinary channels of circulation to other parts of the body. The distribution by lymphatics is a direct consequence of growth into the connective-tissue spaces, since these minute channels open directly into the lymphatics. Hence we find that, after the connective-tissue, the nearest lymph-glands are the first parts to be affected.

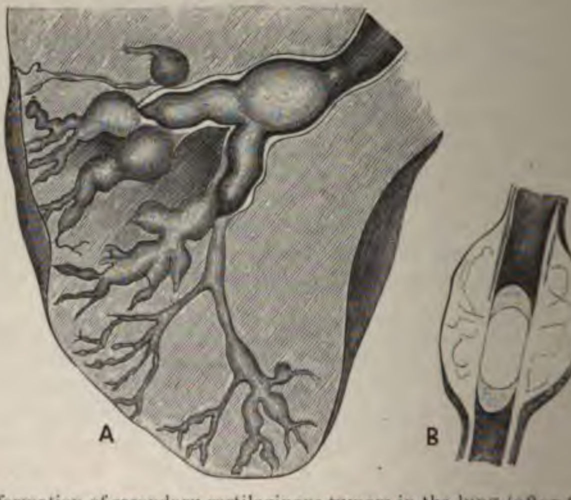
How does the transmission take place? Is it that the advancing columns of cells grow continuously along the lymphatics? Or that small, mobile cells are rolled along with the lymph-current in the same way as ordinary leucocytes? Or is there something transmitted different from cells, which has the power of stirring up secondary growths in the parts to which it is conveyed? It is probable that both the two first mentioned modes of transmission actually operate; though the second is the more usual; but there are no facts in support of the third method. To this topic, however, we must recur again.

Distribution by the blood-channels is effected by the malignant growth pentrating the walls of capillaries or veins, and forming masses inside these vessels, small portions of which, perhaps individual cells, are carried away by the blood-current and lodged in small arteries, pulmonary or sytemic, where they form embolisms (see Chapter VII.). Though the precise mode of distribution is often traced with difficulty, the order of frequency in which different organs are affected by secondary growths, and the anatomical changes in the parts affected, show that this purely mechanical process is the chief factor in the distribution of secondary growths. Thus the most frequent situation of secondary growths is in the lungs, when conveyance takes place by systemic veins. When the primary growth is in organs connected with the portal system, secondary growths are found chiefly in the liver. When the distribution is more general, and the secondary formation or metastasis takes place in such an organ as the kidney, the secondary growth may be traced to the afferent arterioles connected with the Malpighian bodies. In all these respects the phenomena are similar to those of ordinary embolism.

Another argument in favor of this being essentially a mechanical process is that the production of secondary growths is not peculiar to the tumors usually called malignant, or those which have much local infectiveness, but is sometimes, though rarely, observed in the case of simple tumors.

Cartilaginous tumors, for instance, in rare cases, grow into the veins, and thus form embolisms in the lungs, which become secondary tumors. In Fig. 38 is shown a cartilaginous embolism in the pulmonary artery occupying a large and several smaller branches. At B it is seen that such a mass does not remain as a passive block, but grows out through the walls of the vessel in which it is lodged.

FIG. 38.



Mode of formation of secondary cartilaginous tumors in the lung (after O. WEBER).

A, embolic mass of cartilaginous tumor in branch of pulmonary artery; B, similar mass growing through the walls of the pulmonary vessel and forming a secondary tumor.

Of late years several instances have been recorded in which the simple tumor or hypertrophy of the thyroid gland, called goitre or bronchocele, has given rise to secondary tumors precisely resembling the thyroid in structure, neither the primary nor the secondary tumors showing any approach to cancer. In one case a small mass of gland-structure was seen growing into a vein within the thyroid.

Among malignant tumors this mode of secondary distribution is most commonly seen in sarcoma, and the embolic process is often distinctly traceable. Cancers of the abdominal organs often form masses of new-growth, known as cancerous thrombi in the portal vein, from which masses are conveyed into the liver; and cancers of the kidney rather frequently form similar masses in the renal veins.

In all these cases the mechanical nature of the process is unmistakable. When, however, secondary growths are more numerous and widely distributed, the relations are not so obvious; and it has been supposed that the secondary productions are not really metastatic, but result from the same cause as produced the original tumor. But, on the general principle of explaining the obscure by the clear, it is reasonable to suppose, unless there is evidence to the contrary, that process is in all cases the same. Sometimes the embolic particles may be small enough to pass the pulmonary capillaries without being arrested there, and be afterward deposited in other organs.

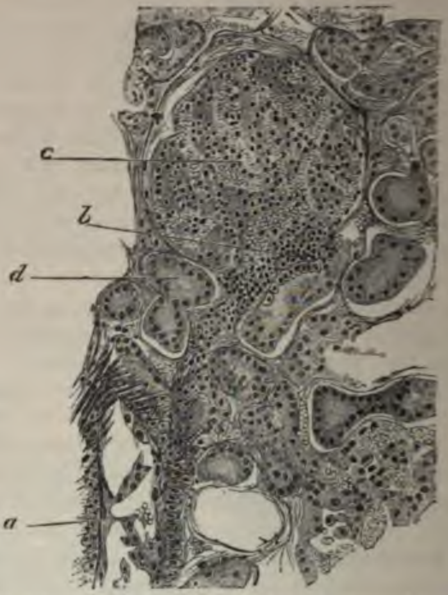
Why some organs rather than others should be the seat of secondary tumors is not clear, but there are probably some affinities not yet explained between the tissues of the primary growth and those of certain other organs, so that, though the cells may be carried to all parts of the body, they only take root and grow in certain parts.

Structure of Secondary Growths.—There is the most striking identity between the structure of the original tumor and that of all those which are formed from it. The most definite forms of cells—such as squamous epithelium, or cylindrical epithelium—and their precise arrangement, as forming, for instance, tubular gland-structure or closed follicles like those of the thyroid, are all reproduced; and, what is still more remarkable, the physiological properties of the tissue also recur again. The epidermis, for instance, retains its tendency to horny degeneration, both in primary and secondary tumors. Mammary gland-structure retains, in secondary tumors, its tendency to fatty metabolism. The form of cancer called colloid always shows, in its metastatic growths, the same colloid degeneration as in the primary tumor, and so in other cases. Consequently it is often possible, from the structure of secondary tumors, to say in what organ the primary tumor originated.

Some of these points are illustrated in Fig. 39, which represents a secondary growth in the kidney, derived from a primary adenoma or tubular gland-tumor of the liver.

An afferent arteriole is seen to contain cells quite unlike its own normal elements. These new cells at two places, *a* and *b*, grow through the wall of the vessel, and appear on the outer side in the form of a cylindrical epithelium. The whole Malpighian tuft and arteriole are studded with nuclei, showing active proliferation, and there is intense hyperæmia. When the growth is complete, it forms a tubular gland-structure like Fig. 40, reproducing the original tumor of the liver. Here we see that directly the metastatic cells begin to grow they recur to their original type, and cause the connective tissue to grow round them so as to form a structure like the primary tumor. Since the new cells must grow in the place of the cells of the organ in which they lodge, such as renal epithelium, they will often appear to arise from transformation of these latter elements; but in the specimen from which the figure was taken, though there were numerous secondary growths, I could never trace any intermediate forms between the renal epithelium and that of the new-growth.

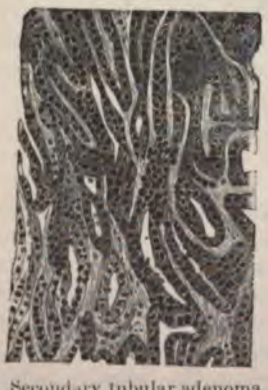
Fig. 39.



Secondary embolic growth in the kidney, derived from adenoma of liver.

a, arteriole containing cells of the new-growth which infiltrate the walls; *b*, smaller arteriole entering Malpighian tuft. From one side columnar cells growing into a uriniferous tube; *c*, Malpighian tuft with abundant nuclei; *d*, uriniferous tubes unaltered. The tissues are engorged with blood.

Fig. 40.



Secondary tubular adenoma of kidney, showing completed structure.

Specific or Parasitic Theory of Malignant Tumors.—The chief arguments in favor of the theory that malignant growths are produced by some specific virus like those of infective inflammations, such as pyæmia or tubercle, or those of specific fevers, are somewhat as follows.

All other alleged causes of tumor-growth in general, or of malignant growth in particular, are inadequate to explain the phenomena which we have called local and general infectiveness. The growth and extension of malignant growths do, on the other hand, resemble the corresponding phenomena in the diseases above mentioned. In the one class, as in the other, the morbid process begins at one spot and spreads in the first instance by direct contiguity to neighboring parts, afterward by the lymphatic and blood-channels to distant parts. It must, therefore, be supposed that in all cases some specific excitant of growth is conveyed from one part to another.

Again, the analogy of the tumors produced in plants by animal parasites, namely, galls and the like, is also quoted to show that tumors may be produced by specific parasites, each of which gives rise to a characteristic kind of growth.

Sir James Paget supposes that there is, in the first instance, a constitutional infection, of which the growth called a cancer is the local manifestation. But the more usual way of presenting the parasitic theory assumes that the disease is local in the first instance, and afterward becomes more or less general.

Against these arguments it is urged, first, that malignant tumors differ from those diseases with which they are compared in not being contagious to man or inoculable on any other animal. The alleged instances of transference of cancer from one person to another are exceedingly rare, and not free from ambiguity. Moreover, very numerous experiments have been made with the object of inoculating cancer or other tumors into animals. Not only have growths from the human body been grafted on animals, but also growths from the same species of animal as that experimented upon, and the experiments have been varied in many ways. The results have, however, been in every instance entirely negative. Sometimes the engrafted tissue has retained its vitality for a short time; but it has not preserved its characters or given rise to any continuous growth. Now, since the final proof that a disease such as tubercle, for instance, is a specific one, and produced by some definite virus, is that it can be transferred from one subject to another, the impossibility of thus transferring malignant tumors is a strong argument, though not a decisive one, against their specific nature.

In the second place, the effect of the known poisons of specific diseases, and especially of microörganisms, is somewhat different from what we see in cancer. Their action is essentially injurious or destructive. They do not cause overgrowths directly, but only produce the reactive growth of inflammation above described. This growth is accordingly limited to the connective-tissue, and is not essentially different from that set up by other injuries. When something in the shape of a tumor is produced, as in the granulation tumors, this is really, as shown elsewhere, a kind of exaggerated scar. But in the most malignant tumors, namely, cancers, the essential part of the process is a primary overgrowth of epithelium, the other tissue-changes being secondary; and no specific virus or microörganism has yet been found which has the power of directly causing an overgrowth of this kind. Hence, it seems improbable that the specific cause of cancer, if there be one, is of the same kind as the causes of the diseases above mentioned.

Many elaborate researches have been made to find out whether malignant tumors contain any parasitic organisms. The latest and among the most complete are those of Messrs. Ballance and Shattock. They took portions of cancerous and other tumors and placed them (adopting methods elsewhere spoken of) in circumstances under which any microörganisms if present would grow. But in no case was any such growth observed. The conclusion was that the tumors contained no microörganisms, and the experimenters, while believing that cancer is caused by some parasite, conclude that if a vegetable parasite be the cause of cancer, it must be one of a very special kind. They suggest that a minute animal parasite may be concerned, though of this there is no evidence.

On the whole, we must conclude it to be improbable that cancer is caused by a microörganism like that of tubercle; but it is not impossible that there may be some specific poison of a different kind. The question can only be decided by the actual discovery of such a poison.

Criterion of Malignancy.—Local and general infectiveness may accordingly be taken as the criterion of what is meant by the malignancy of tumors. The other so-called malignant properties are matters of degree.

The curability or incurability of malignant growths depends very much upon mechanical causes. Epithelioma of the skin has been cured in very many cases by early removal, though, if left alone, it may produce the whole train of malignant symptoms. When occurring on the tongue or other moist parts, prognosis is, according to surgeons, much less hopeful, because the moisture and greater vascularity of the site favor extension of growth into surrounding parts. Mammary cancer has such an extraordinary power of infecting the surrounding parts at an early period of growth, that it is rarely, if ever, successfully cured by operation. But there is abundant evidence that recurrence takes place from small portions of growths infiltrated into the tissues, and hence left behind at the operation. Again, certain forms of sarcoma, especially the spindle-celled, when they occur on the limbs, may be, and often are, completely cured by operation.

Formerly they were not thought to occur in internal organs, and hence a comparatively favorable estimate was formed of their malignancy; but since sarcoma of internal organs has been better studied, it has been found that in these situations such growths are highly malignant, as they cannot be extirpated at an early stage.

Structure as a Criterion of Malignancy.—If the only test of a tumor being malignant is its local and general infectiveness, it is evident that this is not a convenient basis for a diagnosis or classification, since these properties are not always apparent till revealed by the course of events. Hence it has for a long time been the aim of pathologists to discover what structure, if any, is always associated with malignant properties.

An enormous number of researches have been made in this direction during the last twenty or thirty years, of which the results may perhaps be summed up as follows:

1. There is no one kind of structure characteristic of malignant growths.

2. Nevertheless, it may be broadly said that malignant growths are nearly always heterologous or atypical in structure; and that typical or simple growths having such properties are quite exceptional. The only simple tissue tumor which is at all frequently malignant is lymphoma.

3. The great majority of malignant growths fall under one of two heads; either sarcoma on the one hand, or carcinoma on the other. The latter has, as a rule, more definitely malignant properties than the former.

These results do not give a convenient basis for practical rules of diagnosis, but we may argue with great certainty from structure to properties by adopting a somewhat different method.

This method may be described as that of natural history.

It consists in arranging all morbid growths, for purposes of classification and diagnosis, according to structure solely, and not according to properties. Having thus determined the systematic position and name of the growth, we have access to all the existing recorded experience respecting its properties. This experience is now so large that there is usually no difficulty in predicting from the structure of a growth what is likely to be its history, and its effect on the organism, except in the improbable case of our having to deal with an entirely new form of tumor. Just so, in botany and zoölogy, when we have determined the name of a plant or animal, we can learn all that is known about its habits and properties; but we do not find it necessary to classify plants according as they are useful, poisonous or harmless, animals as rapacious or innocent, and so forth. Hence an anatomical or structural classification of tumors is that which has most practical value, as well as the highest scientific completeness.

Classification of New Growths.—On the principles explained above, all new-growths may be classified as follows.

A. MESOBLASTIC TUMORS.

I. *Simple or Typical Tissue Tumors.*

1. Fibroma,
   Variety Glioma.
2. Myxoma.
3. Lipoma.
4. Chondroma.
5. Osteoma
6. Lymphoma.
7. Myoma.
8. Neuroma.
9. Angioma.

II. *Atypical or Aberrant.*
  Sarcoma.

B. Epithelial Tumors.

(Epiblastic and Hypoblastic.)

I. *Simple or Typical.*
  1. Simple epithelial growths.
  2. Adenoma.

II. *Atypical or Aberrant.*
  1. Squamous Epithelioma.
  2. Glandular Carcinoma.

C. Teratoid Tumors.

(Tumors composed of several different kinds of tissue, forming a imperfect organ, or imperfectly developed individual.)

CHAPTER XIX.

SIMPLE TISSUE TUMORS.

1. **Fibroma** or **Fibrous Tumor.**—By this term is understood a tumor composed of fibrous connective tissue.

These may be met with in most parts of the body which normally contain such tissue, but are commonest in the skin; next in the sheaths of nerves, in ovary, periosteum, and fasciæ. They are also found less commonly in the uterus, the mamma, and other glands, as the kidney. But in glandular organs they grow from the connective-tissue stroma, not from the gland-cells. In order to be called fibroma the growth must be a definite node or lump, not a mere infiltration or thickening of preëxisting fibrous tissue. On surfaces, skin or mucous membrane, fibrous tumors often project as a sessile or pedunculated mass, forming a papilloma or polypus, covered by the epithelial investment belonging to the part. The affection called *molluscum fibrosum* furnishes an instance of such growths. It is sometimes combined with a sort of diffuse hypertrophy of parts of the skin, and more rarely with fibrous tumors of other parts, especially of nerves.

Fibrous tumors are broadly divisible into two groups; (1) hard or dense, and (2) soft or loose-textured. The latter have also been called fibro-cellular tumors, but as this term has also been applied to myxoma, it is ambiguous. The former kind are composed of dense interlacing fibrous bundles, sometimes broad and swollen. They may be nearly as hard as cartilage, and may resemble it in appearance. They contain comparatively few cells.

The softer kind are composed of areolar connective tissue, with wider meshes, and contain, as a rule, more visible cells, which show the ordinary forms of fixed connective-tissue corpuscles, with a variable number of migratory cells. There is often also much intercellular fluid, which is albuminous. But all gradations are met with between the one and the other.

In both forms fibroplastic cells are met with, showing the formation of fibrous tissue by proliferation of the matrix or tissue in which the growth originates.

Fibres of elastic tissue are sometimes seen.

Fibrous tumors are subject to degeneration, both mucous and fatty, and in some cases become calcified. In those developed from periosteum true bone may be produced, unconnected with the original bone.

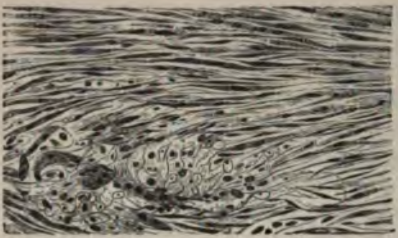
The fibrous tissue is often combined with other tissues, as fatty, myxomatous, cartilaginous, and muscular, forming mixed tumors, or with embryonic tissue, *i. e.*, with sarcoma.

Cysts are sometimes formed in fibrous tumors, especially in mucous polypi; and glands sometimes included in them, so as to produce other mixed forms.

Special names are given to several of the above forms, which explain themselves: as fibro-sarcoma, fibro-lipoma, fibro-myoma, cysto-fibroma, adeno-fibroma, etc.

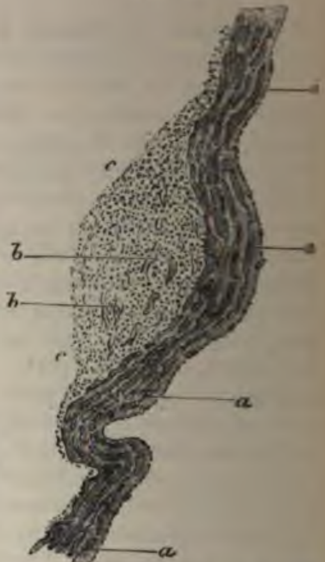
Fibro-sarcoma is best reckoned with the sarcomata; and fibro-myoma, forming the well-known uterine fibroids, will here be described under the head of myoma.

FIG. 41.



Section of fibrous tumor from the skin, showing some fibres cut longitudinally, others transversely.

FIG. 42.



Fibroma in sheath of nerve or false neuroma.

a, unaltered nerve-tubes; *b*, isolated nerve-tubes in the new-growth; *c*, new-growth of connective-tissue starting from perineurium. (Trans. Path. Soc., vol. xi.)

Fibrous tumors in the sheaths of nerves are sometimes called neuro-fibroma or false neuroma. They are quite independent of the nerve-fibres (see Fig. 42).

If we remove the class of fibro-myomata, fibrous tumors are not often very large. Perhaps the largest forms are some connected with the ovaries. They are often very numerous; the pendulous tumors of the skin, called fibroma molluscum, sometimes occurring by hundreds. Fibrous tumors on nerves, called fibro-neuromata, are also often multiple. But it is a singular fact that multiple fibrous tumors are hardly ever met with except in connection with these two tissues.

Fibrous tumors are, broadly speaking, never malignant. They do not infect neighboring parts, or give rise to secondary growths by metastasis; and they are not injurious except by mechanical pressure.

The few cases on record described as "malignant fibrous tumors," were mostly sarcomata, or at least mixed forms; but one or two of genuine fibrous structure have been described.

Glioma, a growth formed by increase of the connective-tissue of the nerve-centres (neuroglia) is, strictly speaking, a simple tissue-tumor, and may be regarded as a variety of fibroma. But it also has points of resemblance to sarcoma, and some forms are undoubtedly sarcomatous.

One peculiar form of fibrous growth, known as *keloid*, or more accurately *cheloid*, must be considered here. The type of cheloid is an ordinary fibrous scar, and most of these growths develop by hypertrophy out of a scar, but there are cases of spontaneous cheloid, not preceded by a wound. The structure is pure fibrous tissue; the form very irregular.

Some persons have a remarkable tendency to the development of cheloid, any wound or inflammatory lesions, such as acne, producing a growth of this structure.

The large tumors, called *elephantiasis* (*Arabum*), formed on the scrotum and other parts are usually reckoned among fibromata ; but some forms certainly are due to parasites, especially the so-called lymph-scrotum or nævoid elephantiasis, produced by a filaria (see Part II.). In other cases no such cause has been proved to exist. The growth consists in immense hypertrophy of the cutis and subcutaneous tissue, with the accompanying vessels, in one or more of the extremities or the genitals. The mass thus consists chiefly of fibrous tissue. Enormous tumors, weighing a hundred pounds or more, have been removed. The disease is endemic in certain countries, chiefly tropical, a fact which, in connection with other evidence, suggests that it may be essentially parasitic.

Glioma.—Hyperplasia of the neuroglia produces tumors which are hardly separable from the surrounding tissue, but form masses which may be as large as a walnut or rarely larger. Their structure reproduces the variations of the normal neuroglia. Most often we see roundish or oval cells imbedded in a granular matrix, and as the protoplasm of the cells is often seen with difficulty, the elements may appear to be merely nuclei. In some forms branded cells, like those described as belonging to the normal neuroglia, are seen. They vary in the degree of vascularity, but are in general poorly supplied with vessels, and hence liable to degeneration, fatty or calcareous. In some cases there is a good deal of hemorrhage, which has sometimes proved fatal. The color is accordingly various, being either grayish and translucent, yellow and opaque, or more or less red. Cysts are often produced by softening.

These tumors are, on the whole, rare, and we have seen few specimens, but Virchow distinguishes a hard and soft form. The hard approaches an ordinary fibroma, containing nucleated connective-tissue; the soft more nearly resembles myxoma, and shows stellate cells.

The nervous elements take no part in its production.

Glioma is generally solitary, its growth is very slow, and the symptoms, if any produced, are merely those of pressure. The part of the brain where it most frequently occurs is in the white substance surrounding the lateral ventricles, especially the posterior cornua, but it may occur elsewhere. It does not extend beyond the nerve-centres, and in the brain, if it reaches the meninges, does not penetrate them. It never gives rise to secondary growths, and is distinctly innocent.

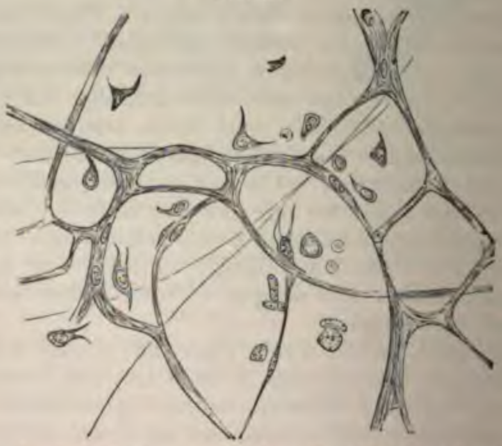
This growth is found chiefly in the brain, more rarely in the spinal cord. Tumors of somewhat similar structure occur in the retina, but as they approach more nearly to sarcoma, they are noticed under that head.

Glioma of the spinal cord is sometimes central, and produces serious symptoms, by pressing on the nervous tissue and dilatation of the central canal. But this is a rare form of growth.

Combinations of cerebral glioma with sarcoma have been met with.

2. Myxoma—Mucous Tumor.—This name is given to a tumor composed of the variety of connective-tissue called mucous or gelatinous tissue. In this the intercellular substance has a gelatinous appearance, is usually semi-solid, and contains, as its chief constituent, mucin, instead of, or in addition to, the serum, albumen, gelatin or chondrin obtained from other forms of connective-tissue. The cells are stellated or branched, their processes being joined together to form a network. This form of tissue is met with normally in the adult body only in the vitreous body of the eye, but also composes the umbilical cord. It also represents the immature condition of fatty tissue occupying the place of the subcutaneous tissue in the fœtus, and also the immature condition of fibrous connective-tissue. To avoid confusion, it is well to point out that it has nothing to do with the mucous membranes.

Fig. 43.



Myxoma, showing stellate or multipolar cells, with trabeculæ of various thicknesses, and a few leucocytes (carmine staining).

The structure of myxoma shows the typical form of areolar connective-tissue, consisting of flat cells with two or more angles connected with prolongations united together so as to form a network. These prolongations may be extremely delicate fibrils, or may be fibrous trabeculæ of considerable thickness, as in the figure. There are besides scattered connective-tissue cells of less mature form, and a variable number of migratory leucocytes. The fixed cells often contain fat globules, and thus there is an easy transition to adipose tissue.

Sometimes there are a large number of immature cells, which form a transition to sarcoma. Thus the only real difference between this and the loose form of fibroma is the nature of the intercellular substance. The chief degeneration to which myxoma is subject is mucous softening, by which portions may become liquefied.

Myxoma is thus really a variety of fibroma, but its near affinity to lipoma is shown by many specimens.

Most myxomata are of a tolerably firm gelatinous consistence, but sometimes the intercellular substance is so liquid as to drain away on section. The color is usually yellowish, like gelatine, but often mottled with red, from abundance of bloodvessels or hemorrhage. They are transparent, or at least translucent, except in parts where there is fatty tissue or fatty degeneration.

These tumors are very frequently mixed, the mucous tissue being most often combined with fatty tissue, sometimes with cartilage, sometimes with fibrous tissue, and again in many cases with sarcoma. The last-named combination often determines the character of the growth, causing it to recur and to be in some degree malignant.

Thus a tumor of this kind may give rise to secondary growths in other organs, but these secondary growths will be sarcomatous, not myxomatous. Otherwise they are as innocent as fibrous tumors.

Myxoma grows from various forms of connective tissue, often from one of the situations of fatty tissue, also from intermuscular septa and fascia, and not unfrequently from glands, more especially the parotid, in which a very characteristic form of tumor, composed of myxoma mingled with cartilage, and often with sarcoma-structure, is found.[1]

Some polypi of mucous surfaces appear to have the structure of myxoma.

The remarkable formations known as uterine moles or uterine hydatids, produced by a peculiar degeneration of the placenta, have also been shown by Virchow to have the structure of myxoma.

3. Lipoma or Fatty Tumor.—Growths composed of fatty tissue are among the commonest of simple tumors. This tissue, being one disposed to vegetable growth, and liable to rapid increase or wasting, is particularly adapted to tumor-growth. These tumors often grow to a great size, and are sometimes multiple.

The largest tumor on record belongs to this class. A drawing of it only is preserved in the Warren Anatomical Museum, Boston, U. S. It was estimated at about 275 lbs.; the weight of the subject, a woman, without the tumor, being estimated at less than 100 lbs.

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[1] The specimen figured above was taken from a very large myxo-lipoma of the gluteal region, which was remarkable as having grown on the site of a fatty tumor previously removed. It shows the structure as seen without any hardening. Hardened and contracted specimens look very different (Trans. Path. Soc. xx. 343).

Others are recorded as having weighed 20, 30 or even 55 lbs. (Cooper Forster) and more.

These growths are sometimes very numerous. Multiple fatty tumors are not uncommonly observed on the surface of the body, to the number of twenty, thirty, or more. In one remarkable case recorded by Broca no less than 2080 were counted, which were believed to be secondary.

However large or however numerous, fatty tumors always grow from preëxisting fatty tissue.

The apparent exceptions to this rule are explained by the occurrence of adipose tissue in unusual situations, as within the spinal canal, or by the growth of the tumor from its original seat into a neighboring cavity. The latter is seen when a growth from the subserous fatty tissue penetrates into the peritoneum, or one from the submucous projects on a mucous surface.

Adipose tissue is remarkably prone to hypertrophy, and there appears to be sometimes a connection between excessive production of fat, or obesity, and fatty tumor. The latter sometimes occurs at the time of life at which corpulence begins, and sometimes in corpulent people; but often the conditions are reversed, or no connection can be traced. Generally speaking, no cause can be assigned for the production of a fatty tumor. In a few cases, traumatic influence, such as friction, may be regarded as having some influence.

The form of fatty tumor may be either a solid mass or pedunculated, like a polypus. In either case the growth is composed of a number of small lobules, held together by highly vascular connective-tissue. One remarkable form, called diffuse lipoma, consists of irregular, ill-defined masses without a capsule, intermediate between a true tumor and ordinary hypertrophy of adipose tissue. It has occurred for the most part in excessive drinkers, and is most always situated on the nape of the neck, submaxillary regions, and shoulders, and arranged with remarkable symmetry.

Metamorphoses.—Fatty tumors are liable to calcification, cystic degeneration, and ulceration. The cysts in them appear to be formed by a softening process. They sometimes contain oil; more generally serous fluid.

The fatty tissue is not unfrequently combined with other forms of connective-tissue, especially fibrous, as mentioned above, and sometimes with myxomatous tissue. There are also instances of combination with sarcoma. In the latter two cases the history of the growth may be expected to be that of myxoma or sarcoma respectively.

With the exceptions just mentioned, fatty tumors are strictly innocent. They do not recur after removal, or give rise to secondary growths, or cause constitutional debility, or produce inconvenience, except by mechanical pressure.

In the very few cases where secondary growths are recorded, such as Broca's case mentioned above, there may probably have been some combination with sarcoma in the original tumor.

4. Chondroma or Enchondroma.—Cartilaginous Tumor. Tumors composed of cartilage may reproduce the several varieties of normal cartilage, but those of hyaline cartilage are the commonest.

These tumors would seem at first to constitute an exception to the law of homologous growth, since they very rarely take their rise from permanent cartilage, and, in fact, considerable cartilaginous tumors never thus originate. But this exception is easily explained. Cartilage being a non-vascular tissue has no power of giving nourishment to a new-growth. It is a barren soil. Growths which originate in it reach no great size.

Certain outgrowths of permanent cartilage are not unfrequently observed, which have received the distinguishing name of *Ecchondrosis.* They represent a simple hyperplasia of the structure, and are with difficulty separated from mere enlargements. They seldom take the form of distinct tumors, and when they do so, do not reach any considerable size, being usually not larger than a pea: the largest described being of the size of a walnut or thereabouts.

They have been found on the cartilages of the ribs, where small outgrowths of cartilage are very common, also on synchondroses, such as the pubic symphysis, on the intervertebral cartilages, and on the cartilages of the larynx and trachea. They are not generally of any importance. Sometimes they become ossified and appear as bony outgrowths.

A remarkable form of ecchondrosis is seen in the "free cartilages" of joints, which have a special surgical interest. Though these do not probably all originate in the same way, some are apparently cartilaginous outgrowths which first become pedunculated, and then detached.

Enchondroma, or cartilaginous tumor properly so-called, may arise from various forms of connective-tissue. Three-fourths or four-fifths of all cases, according to C. O. Weber, originate in bone (but not from the articular cartilages).

The remainder originate in fibrous connective-tissue, such as muscular fasciæ, etc., or more often from certain glands, among which the testicle and the parotid are most often affected.

A considerable number, about one-half, of such tumors have their starting-point in some injury, such as a fracture of bone. In enchondroma of the testicle the proportion of cases with a traumatic origin is still larger. Virchow many years ago suggested that chondromata of bone might originate in masses of primitive cartilage which had remained unossified, and more recently has demonstrated the existence of such isolated masses of cartilage in mature bone. We must, then, suppose that the injury chances upon such a mass of cartilage, which, in consequence, becomes vascularized and grows.

They are sometimes multiple, this peculiarity being especially seen in cartilaginous growths of the fingers; sometimes in other bones. The proclivity to produce such multiple enchondromata is sometimes hereditary.

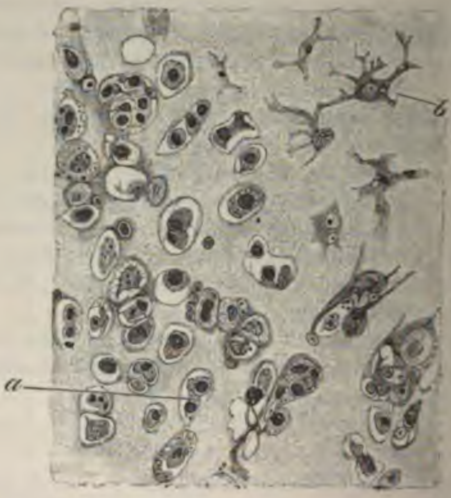
Other mixed forms are found, containing fibrous tissue mixed with the cartilage, or again containing sarcomatous tissue. In the latter case the properties of the tumor are mainly determined by the sarcoma.

Metamorphoses.—Calcification of the cartilage may occur and also the formation of true bone.

Retrograde changes also occur. Softening is very common, the result of which is to form in the interior of the tumor *cysts*, and on the surface a sort of *ulceration*. The cysts may attain a large size; they are especially seen in enchondroma of glands. But it is not certain that all cysts are thus formed. They may be part of the original structure.

Structure.—These tumors are mostly of rounded outline. They are surrounded by vascular fibrous tissue, forming a sort of capsule. The same tissue permeates the growth, dividing it into a number of small masses or islands of cartilage, which are non-vascular, like ordinary cartilage. It is only in this way that a large mass of cartilage could be nourished. Hence, a large cartilaginous tumor is a sort of agglomeration of small ones.

FIG. 44.



Hyaline enchondroma, showing cells of various shapes.

a a, cartilage-capsules containing either one cartilage-cell, or groups of such cells apparently formed by division or masses of embryonic tissue with very minute cells, or combinations of these; and some approaching the stellate form. *b*, stellate cartilage-cells. (These have been transferred from a more distant part of the section, in order to bring them into the field of view.)

The minute structure shows the three chief forms of normal cartilage:

1. *Hyaline*, in which the intercellular substance is clear and homogeneous.

2. *Fibro-cartilage*, in which that substance is fibrillated. The cells

in these two kinds are the same. They are enclosed in a capsule, and the true cell often, when fresh, shows amœboid movements or changes of form. In the other form—

3. *Stellate*, the cells show delicate processes giving a star-like shape. This variety is soft, and often jelly-like in appearance. It constitutes a transition to mucous tissue or myxoma, and tumors are often met with containing both structures, called myxo-chondroma or chondro-myxoma.

The intercellular substance is here semi-fluid, and may yield mucin as well as chondrin and gelatin, which are found in the other forms.

Even in the hyaline variety the form of the cells is not always simple. We often see groups of cells evidently formed by division. More rarely (as in the figure) small masses of embryonic tissue are seen. It may be doubted whether these are of earlier or later formation than the normal cartilage cells; but a careful study of them seems to show that they merely replace those cells without showing any transition. They appear to show a passage to sarcoma-structure; for if the embryonic tissue increased and the intercellular substance disappeared, the tumor would become round-celled sarcoma.

The appearances, it should be said, are quite different from those of inflammation of cartilage.

Mode of Growth.—Cartilaginous tumors extend by a conversion of the surrounding connective tissue into cartilage, through formation of successive new foci. Nevertheless, this process has limits. Enchondroma of bone rarely breaks through the periosteum; that of testicle does not spread outside the gland. In very rare instances has a sort of infection of neighboring tissues been observed. It follows that these tumors affect surrounding parts only mechanically, with rare exceptions. In a few instances cartilaginous growth has been found making its way into the veins of the part; and it may then, through being mechanically conveyed to the lungs, or rarely to other parts, give rise to secondary growths (*see* Fig. 38).

Special Forms of Chondroma.—Of the large class which grow from bone, most arise in the limbs, especially in their extremities, so that they become less frequent as we pass from the periphery to the centre—hands and feet coming first, long bones of the limbs next, central portions of the skeleton last in order of frequency. They generally begin in the *interior* of bones (hence the term *Enchondroma*), but a few start in the peripheral layers of bone, or, as some think, in the periosteum.

The further consideration of these points belongs to surgery. The form called by Virchow osteoid-chondroma is here regarded as a form of sarcoma.

Chondroma of the Testicle is a very remarkable form. It is generally combined with myxoma or sarcoma-structure, generally contains cysts, grows rapidly, and often has its starting-point in some injury. It grows entirely from the connective-tissue of the gland, the tubules being unaffected except by pressure.

Similar growths have, though very rarely, been seen in other parts of the genito-urinary tract—viz., the ovary and kidney.

Chondroma of the parotid is always a mixed tumor, containing myxoma-structure also, and occasionally sarcoma. It is sometimes formed near, sometimes in, the parotid, but the gland-tissue takes no part in the growth, which starts exclusively from connective-tissue. It has been supposed that a mass of embryonic cartilage belonging to the rudimentary pinna of the ear has become lodged in or near the rudimentary parotid gland.

Chondroma of lymphatic glands is met with only as a secondary tumor depending on cartilaginous growth elsewhere. As such it is very rare.

Chondroma of the lung is usually a secondary growth, and this is very uncommon. Still, there are primary cartilaginous tumors of this organ, though very few have been observed. They start mostly in the hilus of the lung, and have been supposed to grow from the bronchial cartilages, but the connection is not clear, and analogy does not make it probable.

Malignancy.—The immense majority of cartilaginous tumors are perfectly innocent, can be removed without recurrence, or, if they return, do not spread to adjacent tissues or to distant parts. In a very few cases, however, the growth has spread to the next lymphatic glands; in a still smaller number, growth has penetrated the veins and thus become conveyed to the lungs; in one or two cases a distinct infection of the adjacent connective-tissue has been observed. There are also cases of secondary cartilaginous tumors in the lung, where the channel of communication was not obvious, though it must have been through the venous circulation. But all these cases taken together make up a very small proportion of the whole number. We must say, then, that chondroma shows malignant properties in rare and exceptional cases only.

5. Osteoma—Bony Tumors.—Bony growths may, like those from cartilage, be divided into two groups, viz., mere outgrowths from existing bones, which may or may not assume the form of a distinct tumor, the so-called *exostoses;* and *heterologous osteomata*, or bony tumors occurring in soft parts. Besides these, we distinguish a class of bony productions called *osteophytes*, which are not true tumors.

Exostoses may reproduce the structure of both kinds of normal bone, spongy or compact. The latter sometimes assumes a remarkably dense hard structure containing few vessels, and are known as ivory exostoses; they are commonest on the skull.

Some appear to begin with a cartilaginous growth which afterward ossifies, and are called *cartilaginous exostoses.* The cartilage continues to grow and become ossified on its inner side, depositing successive layers of bony tissue on the existing exostosis.

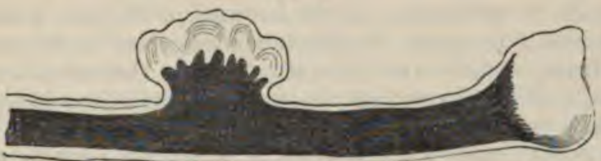
Spongy exostoses form a mass of spongy bone directly continuous with the cancellous tissue of the bone from which they grow. Therefore, though very various in shape, they must be regarded as formed by simple hyperplasia, and are sometimes scarcely distinguishable from hypertrophy.

Exostoses sometimes occur in very large numbers, affecting nearly every bone in the body. They grew in these cases chiefly from certain special situations—near the articular extremities of the long bones, on the ribs near their junction with the cartilages, and so on, in fact near the epiphyses, and at the same parts as those which are affected in rickets. On this ground it has been assumed that these multiple exostoses have some connection with rickets, but of this there is no evidence; except that masses of cartilage are sometimes, as mentioned above, left unossified in rickety bones, and might become the starting-point of new-growths. Probably exostoses grow from the residues of embryonic cartilage left in the formation of the bone (as in the case of chondromata), these becoming ossified in the process of growth.

The production of these multiple growths always takes place in early life, the recorded cases varying from the second to the twenty-first year; that is, generally speaking, before the ossification of the skeleton is complete, and mostly about the age of puberty. Accordingly the supposition has been made that the growth takes place from the cartilage of the epiphyses, which in such situations as the lower end of the femur are still ununited with the shaft. However, they occur also in other situations; *e.g.*, at the junction of a rib with its cartilage.

The structure, in almost all cases, has been the same as in one observed by the author; viz., cancellous bone capped by a layer of hyaline cartilage, the whole being covered by periosteum.

FIG. 45.



Cartilaginous exostosis of rib, partly converted into cancellous bone (after O. WEBER).

In some cases a bursa has been found developed over the tumor, but not necessarily in communication with the joint.

There are some reasons for thinking that these exostoses may all have been cartilaginous in the first instance, and have been formed by a gradual ossification, as above described. This is confirmed by the observation that cartilaginous outgrowths are found in the same situations, and in some cases bony and cartilaginous tumors have been found simultaneously; so that both must be regarded as the outcome of the same tendency.

The cause of these multiple growths is unknown. No connection with any diathetic disease can be made out. The tendency to produce them is sometimes hereditary, giving rise, in the same family, sometimes to bony, sometimes to cartilaginous, tumors. They cease to grow after a time and remain passive for the rest of the patient's life. In one instance febrile symptoms accompanied their growth.

Heterologous Osteomata are bony tumors formed in organs quite unconnected with bone. They are very rare. They have been observed in the brain quite unconnected with the skull or membranes, and arising from a metamorphosis of the neuroglia.

Bony tumors have also been found in the eye, on the choroid, and in the vitreous body. It is notable that in wasted or destroyed eyeball, plates of true bone are sometimes formed, which the writer can confirm from personal observation.

Primary osteoma (not to be confounded with secondary osteo-sarcoma, which will be afterward spoken of) has also been seen, very rarely, in the lungs, and is comparable to primary enchondroma of the lung.

Equally uncommon and curious is the occurrence of small osteomata in the skin.

Osteophytes are masses of bone developed in tendons, fasciæ, muscles or other tissue connected with bone, but which are not regarded as outgrowths of the bone itself.

When the bone is macerated, these osseous masses, often of very irregular shape, appear continuous with it; though they may have been originally separate. They may be recognized by being developed at the point of insertion of muscles, tendons, etc., so that they may appear like enlargements of the normal prominences or ridges of the bone.

They are sometimes developed by friction or excessive tension, and hence have been seen in the adductors of the thigh in those who ride much (*e. g.*, cavalry soldiers), or in the tendon of the deltoid near its attachment to the humerus of the left arm in German soldiers from the pressure of the gun. Similar formations occur in the membranes of the brain, notably the dura mater, from chronic inflammation. Closely allied to these are inflammatory new-formations of bone which are formed round fracture or after periostitis, producing a structure like the callus produced for purposes of repair, but permanent. Such a structure may be formed by overgrowth of ordinary cells.

It is, however, difficult to draw the line between all these forms and true exostoses.

True osteomata are in all cases innocent. No instance is known of the production of secondary tumors. But sarcomata growing from bone and containing bony tissue may be malignant.

CHAPTER XX.

SIMPLE TISSUE TUMORS.—(*Continued.*)

Lymphoma or Lymphatic Tumor.—By this is meant a tumor composed of lymphatic or cytogenous connective-tissue, also called adenoid tissue.

This tissue consists of a reticular stroma containing a very large number of leucocytes, corresponding to the ordinary migratory corpuscles of connective-tissue. There are also nuclei which appear to belong specially to the reticulum. This tissue is found in a diffuse form under the mucous membrane at various parts of the respiratory and of the digestive tract. It is sometimes collected into masses, called at different parts tonsils, pharyngeal tonsils, lenticular glands of the stomach, solitary or agminated glands of the intestines, etc. It also makes up the bulk of the thymus gland, the Malpighian corpuscles of the spleen, and a large part of lymphatic glands, viz., the lymph-follicles of the cortex and the medullary cylinders; and is found also in other parts of the body, as described in the manuals of histology.

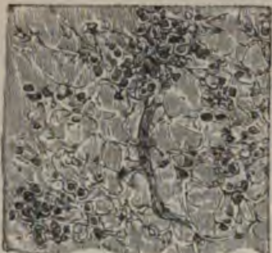
It would seem that the bulk of this tissue is subject to considerable variations, even from physiological causes; and it is certain that slight pathological influences, such as a low degree of inflammation, or simple hyperæmia, may increase it.

Increase of the above described tissue in the form of a tumor is called lymphoma, but since most of such tumors are formed from lymphatic glands, they are really hyperplasia of those structures, and are not clearly separated from simple enlargement. They are distinguished from inflammatory enlargements of such glands chiefly by their permanence. Hence the name of new-growths is not strictly applicable to them; and the term lymphoma is not strictly appropriate. It is, however, often used for overgrowths of lymphatic glands not caused by inflammation or by any obvious cause; and is therefore introduced here for the sake of explaining the meaning of the term.

Multiple lymphatic tumors are, however, met with, in which not only the lymphatic glands, but also masses of cytogenous tissue in other parts, undergo hyperplasia. This condition is known by the name of Hodgkin's Disease, *Adénie* or *Anæmia lymphatica.* No distinct line can be drawn between these productions and lympho-sarcoma. The name lymph-adenoma has also been used, but in practice means the same as lymphoma.

The increase of bulk appears to take place, at least, in part by emigration of leucocytes out of the bloodvessels into the cytogenous tissue; just as in the case of the ordinary migratory cells of connective-tissue. It is also highly probable that adenoid tissue may be formed in parts where it does not normally exist, by the same process. The formation of similar tissue by the production, on the spot, of new lymphatic elements or leucocytes, though it has not been proved to take place, is highly probable, especially in those structures which are believed normally to furnish leucocytes to the blood.

Fig. 46.



Stroma of a lymphatic tumor, with most of the leucocytes removed, showing the nuclei of the stroma. (Drawn with dark ground illumination so that the fibres look bright.)

Pathological cytogenous tissue is, in general, like the normal, but shows, in some cases, certain differences. 1. The reticular stroma may be very small, hardly perceptible, or it may, on the other hand, be much increased, consisting of broad fibrous bands, so that the cells are subordinate.

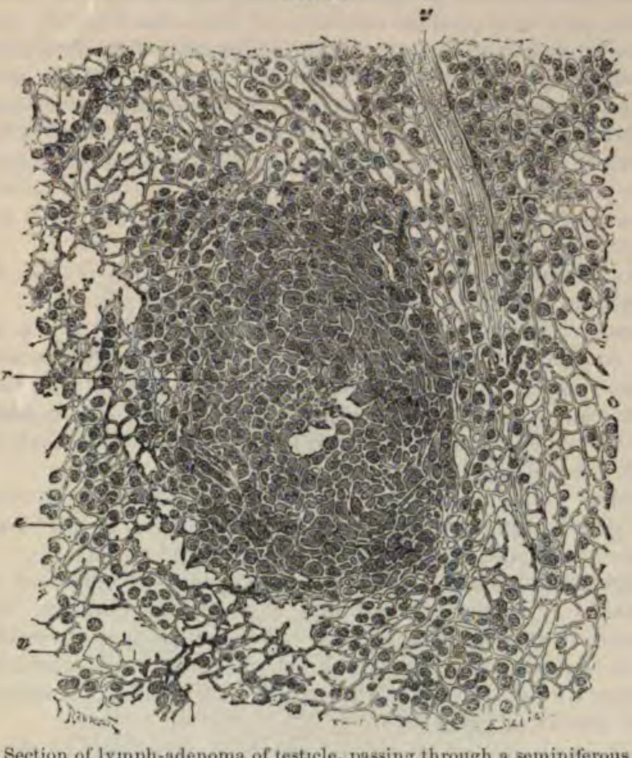
2. The nuclei of the reticulum are sometimes very abundant.

3. The cells may be various in shape, larger than leucocytes and departing from their type; large myeloid cells are not uncommon. Such forms approach the structure of sarcoma, and it is extremely difficult to draw the line. They have been called lympho-sarcoma, and especially belong to the *hard* form as distinguished by Virchow; but it is important to remember that all the changes mentioned above may be found in chronic inflammation of lymphatic glands, and hence, cannot be held distinctive. The term lympho-sarcoma has also been given to lymphatic tumors of very simple structure, which possess locally infective or malignant properties. Hence we find it impossible to draw the line between lymphoma and lympho-sarcoma; and describe all forms under one head, only laying down the general principle that tumors of this kind, even when very simple in structure, may have the malignant properties of sarcoma and carcinoma.

Multiple Lymphomata.—These productions, in which tissue of one kind is multiplied in the form of new-growth in various parts of the body, may be compared to multiple exostoses, or other multiple simple tumors. There is, however, this difference, that lymphatic growths may be secondary or metastatic, and it is not always easy to say which are primary and which are secondary. Generally we may suppose that those occurring in the original seats of the lymphatic tissue, lymphatic glands, and the follicles of the spleen, may be primary, and those occurring in parts where no such tissue is normally found, as the kidney and liver, may be secondary. The latter are always simple in structure.

In a typical case of this kind the following are the appearances met with. Groups of lymphatic glands in various parts of the body are enlarged, often adherent together and forming irregular masses of considerable size. External glands are more often hard, internal often soft and "medullary" in appearance. The minute structure may be that of a normal gland, or may show any of the modifications mentioned above. Masses of lymphatic tissue are also generally found in the spleen, some roundish or angular, and others wedge-shaped. The latter are rather diffuse infiltrations than tumors, and, having the shape of infarctions, are possibly secondary. Masses of similar tissue may be found in the submucous tissue of the intestines, the tonsils, etc.; also less commonly in the liver and kidneys; rarely in other organs. The lungs appear to be never affected, or only in one or two recorded cases, and then by direct contiguity.

Fig. 47.



Section of lymph-adenoma of testicle, passing through a seminiferous tube (Cornil and Ranvier).

r, section of seminiferous tube, with its wall thickened and converted into cytogenous tissue, and some free cells in the cavity; *e*, fibres of reticulum; *n*, lymphatic cells. Magnified 300 diameters.

While it is, therefore, probable that some of these growths are primary and some secondary, there is no proof of actual metastasis or transferrence of particles by the general circulation from one part to another, except, possibly, from the spleen to the liver; otherwise the lungs could hardly escape.

The secondary lymphatic masses formed in various organs in leucæmia much resemble these, but are very simple in structure, consisting of a mass of leucocytes with little or no reticulum. Putting aside the case of the spleen, they may be regarded as merely deposits formed by extravasated leucocytes.

Mediastinal Lymphoma.—The softer forms of lymphoma, with little stroma, are called soft lympho-sarcoma by Virchow. One well-marked form is that which sometimes occurs in the bronchial glands at the hilus of the lung, or in the anterior mediastinum in the situation of the thymus. It is soft, and composed of little else than leucocytes, with a delicate stroma.

These growths often penetrate the lung by a process of continuous infection, and thus produce one form of what was formerly described as primary cancer of the lung. The infiltration also often extends to the pleura or pericardium; and in these cases the growth may soak through (without destroying) the latter, and sometimes even penetrate the heart-wall in the same way, projecting into the cavities in the form of a tumor. They may also surround and press upon the great vessels and air-passages.

These growths, by their locally infective properties, show a highly malignant character, though so simple in structure.

It is noticeable that they occur in a locality which is often the seat of congenital tumors of mixed structure.

In one case a similar tumor was found in front of the sacrum, where congenital tumors also occur. Occasionally soft growths, of lymphatic appearance, have been observed in the skin, forming the very rare and curious disease called *mycosis fungoides* or *granuloma fungoides*; but I cannot agree with Cornil and others that this is a form of lymphoma.

Another well-marked clinical form is lymphoma of the retro-peritoneal glands, formerly called retro-peritoneal cancer. It may press upon the pancreatic and hepatic ducts, or on the portal vein.

Hodgkin's Disease, or Anæmia Lymphatica.—The clinical features of multiple lymphomata were first observed by Hodgkin in 1832. They are: (1) extreme anæmia, the red corpuscles being greatly diminished in number, the leucocytes not increased; (2) cachexia; (3) sometimes dropsy and hemorrhages. To these must be added intercurrent attacks of pyrexia.

Other local symptoms will be produced according to the organs affected in each case.

Some cases of this disease end in acute tuberculosis, which raises the suspicion that the original affection may have been primary tuberculosis of the lymph-glands.

It is not impossible, and in some cases probable, that the soft lymphomata may be produced by some infective poison; and thus come under the head of infective granulomata, but no such poison has yet been traced.

7. Myoma or Muscular Tumor.—There are two varieties of muscular tumor, corresponding to the two kinds of muscular tissue, striped and unstriped, called respectively Rhabdomyoma and Leiomyoma.

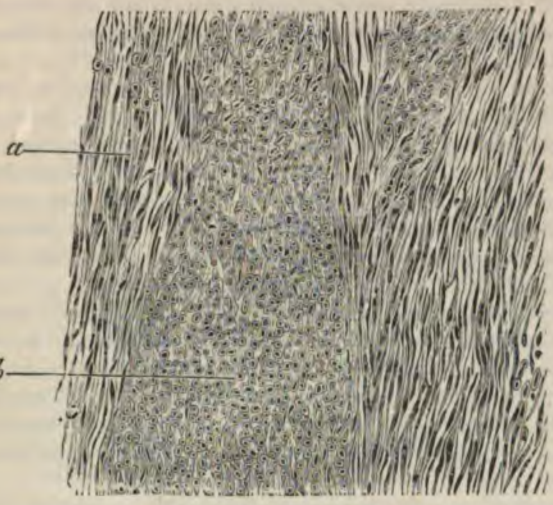
Rhabdomyoma.—Tumors of striped muscle are exceedingly rare. Those wholly composed of this tissue are known only as small *congenital* growths from muscular organs, and, as at present known, are confined to the tongue and the heart.

Muscular growth in the tongue makes part of the condition called macroglossia. In some of these cases considerable masses of muscular tissue are found; but as there is generally some other tissue (*e. g.*, lymphatic) and the growth is not clearly isolated, it hardly deserves the name of a tumor.

In a few cases small round tumors composed of striped muscle have been found in the hearts of children dying soon after birth, or born dead.

Mixed tumors containing striped muscle have been found very rarely in internal organs, not obviously congenital. Several cases are recorded of such a growth in the kidney, mixed with sarcoma-tissue; and of similar construction in the testicle, and once at least forming part of an ovarian cyst. The muscular fibres were in part embryonic, in part fully formed.

FIG. 48.



Section of muscular tumor of uterus.

a, muscular fibres cut longitudinally, showing the oblong nuclei; *b*, the same cut transversely.

The occurrence of muscular fibre in these situations is explained by Cohnheim as the result of a misplacement during fœtal life of embryonic tissue belonging to the proto-vertebra into the mass which forms the rudiment of the urogenital tract. These portions of embryonic tissue are indeed at an early development very closely connected together, and various considerations make this hypothesis very probable. The proto-vertebra, it should be remembered, gives origin to the muscles as well as to cartilage and bone.

The other cases known of striped muscle tumors are too rare and exceptional to be discussed here.

Leiomyoma.—Tumors of unstriped muscle are found in various parts of the body where this tissue normally occurs, but far more frequently in the uterus than anywhere else.

The muscular tumors of the uterus always contain some fibrous tissue as well as muscular, and resemble fibrous tumors in appearance, so that they were formerly called uterine fibroids. Their true nature may be seen on fine sections stained with carmine or logwood, when the rod-shaped nuclei of the muscular tissue become evident. The structure might be taken for spindle-celled sarcoma, but the nuclei of the latter are oval, and show brilliant nucleoli. Perhaps a still better method is to tease out a small portion of the tumor and isolate the fibre-cells by soaking in dilute nitric acid (20 per cent.).

The muscular bundles are woven together in a very complex manner; the tissue is poorly supplied with vessels and sometimes contains cysts. On section we seldom see long muscular fibres, since from their wavy course they are irregularly cut by the plane of section; but on teasing out with dilute nitric acid, the flat fibres are plainly seen. The only distinctive point of structure is the presence of the oblong rod-shaped nuclei.

These tumors when young are almost wholly muscular, and have been observed during life to be capable of contraction. They enlarge with the uterus in pregnancy; but whether they diminish in size again, concurrently with the involution of the uterus, is not known.

The longer such a tumor lasts, the more does fibrous connective tissue enter into its composition, and the harder does it become. In process of time they often become calcified, and have been found as stony masses associated with a skeleton in old graves.

They may be completely imbedded in the uterine wall (intra-parietal), or may project into the pelvic cavity (subserous) or into the uterus (submucous). The two latter forms may become pedunculated, forming polypi of the uterus in the one case, and movable abdominal tumors in the other. The abdominal form may even become separated from its peduncle and constitute a "free body" in the peritoneum.

Of other organs, the stomach most frequently gives rise to smooth muscle-tumors from its muscular walls; the intestine less frequently, and here they are of less considerable size. These growths also occur in the walls of veins, and sometimes in the skin. Some of the growths described as "painful subcutaneous tumors" are of this kind.

Uterine myomata are sometimes very large, weighing several pounds. Considerable tumors have, in rare cases, been found in the stomach. Those of other organs are small.

Leiomyoma is a strictly innocent growth; does not recur or become reproduced in other parts. The tumors are injurious only (though sometimes in a high degree) by their size and position. They belong to late adult life rather than to early life.

8. Neuroma or Nerve-tumor.—New-growth composed of nerve-tissue is extremely rare, and it may be doubted whether any true new-growth, in the sense here spoken of, exists. At all events only a very few isolated cases would come under this category. These have been seen in the brain and in the peripheral nerves.

In the brain, isolated tumor-like masses of gray or white substance are occasionally met with on the surface of the cerebral ventricles, which appear to be of congenital origin, and are associated with congenital hydrocephalus and imperfect development of the brain. They may reach the size of an egg, but are of no practical importance. Even when found at a later period of life they were doubtless congenital, and are no evidence of new-growth of brain-substance. They are rather to be considered as a sort of partial hyperplasia.

Virchow has described some cases of tumors composed of non-medullated nerve-fibres. They are, however, with difficulty distinguished from fibrous tumors.

Fibrous Tumors of Nerves.—On peripheral nerves tumors are found which have for a long time borne the name of *neuroma*, but which are certainly not mainly composed of nervous tissue. They, are, therefore, better called *false neuromata* or *neuro-fibromata.*

These tumors are chiefly of the species fibroma and myxoma. They may seem to be formed in the course of a nerve, and have nerve-fibres running through them; but on minute examination it is seen that the nerve-tissue passes through the new-growth unchanged, or at most separated and expanded. There is no evidence of new growth of nerve-fibres (*see* Fibroma).

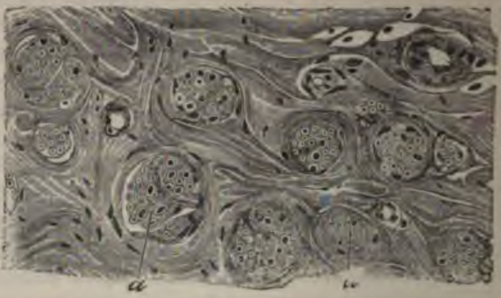
These false neuromata present many remarkable characters. They are often multiple, sometimes occurring by hundreds or thousands, and besetting, in rare cases, every nerve in the body. The tendency to produce them seems often hereditary. They are sometimes associated with fibroma molluscum of the skin. Some tumors of nerves similar in appearance have the structure of myxoma.

Neuroma of Stumps.—In the stumps of amputated limbs, a remarkable swelling of the cut extremities of the nerves is sometimes seen, which has also received the name of neuroma.

These swellings may be as large as a bullet or even larger. Their structure is made up to a large extent of medullated nerve-fibres, which are evidently continuous with those of the cut nerve. It is thus evident there is hyperplasia, though we can hardly call the structure a new-growth.

When a nerve is divided, an outgrowth of nerve-tissue takes place from both ends, but is much more conspicuous on the central than on the peripheral extremity. The nerve-tumors of stumps may be taken as an exaggerated instance of this process. In these we may see nerve-fibres in various stages of development, some small and rudimentary, showing that there is a new formation of nerve-tissue. But there is also a large amount of newly-formed fibrous tissue, derived from the nerve-sheaths.

FIG. 49.



Section through neuroma of an amputation-stump (specimen sent by DR. SHARKEY). *a a*, groups of nerve-fibres cut transversely, showing the fibres in the various stages of development, and embedded in masses of nucleated fibrous tissue.

9. Angioma or Vessel Tumor.—By this is meant a tumor composed of vessels. Two forms are included under this head, viz., those made up of bloodvessels and of lymph-vessels respectively. The former is generally called simply angioma, the latter lymphangioma.

Blood-vascular tumors have to be distinguished from mere expansions of arteries, as aneurisms, and also from the agglomerations of small arteries and capillaries called cirsoid aneurism. These are not tumors in the sense in which the word is here used. There are only two structures here considered, viz., *capillary angioma*, also called *teleangiectasis* (= dilatation of end-vessels or capillaries), and *cavernous angioma*.

In the former, at least, there is a new formation of bloodvessels. In the second there may be sometimes only dilatation and alteration of previously existing blood spaces, but since it is a distinct tumor, it is placed here, even though it is not certain that there is any actual new-growth.

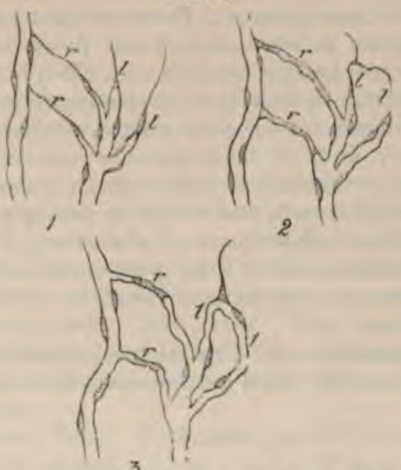
This seems the best place to explain the new formation of vessels in general.

In the embryo the first formation of bloodvessels takes place by the hollowing out of solid, nucleated, protoplasmic cells, which become converted into tubes. The precise relation of the contents of the bloodvessels (*i. e.*, blood corpuscles) to the tubes is still a matter of controversy, which need not be considered here. In the adult body, in normal or pathological states, the new bloodvessels are always formed from preëxisting bloodvessels, and the blood which enters them is the already formed blood. This, therefore, is the only case with which we have here to deal.

This first step is the outgrowth from the protoplasm of the vascular wall of a conical bud or offshoot, composed of solid granular protoplasm. The formation of such an outgrowth was observed by Arnold, in the living tissues of the tadpole's tail, to occupy from two to four hours.

Such a sprout may, while still connected with the original vessel, become partly excavated, its cavity standing in communication with the cavity of the original. Or it may become united, as a solid rod, with the wall of an adjacent vessel. Or two such solid offshoots may unite, forming a solid arch, and secondary buds may start from the first, so that a branched solid structure is produced. In any case the solid protoplasmic rods thus formed become in the end excavated and converted into tubes. These tubes or rudimentary capillaries have at first quite simple walls, but soon nuclei are developed in them, and the area of protoplasm round each nucleus becomes defined, till the wall becomes converted into a structure of endothelial cells connected by cement substance—in fact, into a normal capillary. This process has been observed to be completed in ten or twelve hours.

FIG. 50.



Development of new bloodvessels in the tadpole's tail (ARNOLD).

1. Two capillaries connected by protoplasmic threads, *r r*, one of them giving off free protoplasmic processes, *l l*. 2. The same after six hours; *r r* have become solid rods, *l l* have joined together to form a loop. 3. The same after ten hours; *r r* nearly, *l l* completely channelled so as to form new vessels.

When a simple capillary is thus formed, its wall may be thickened by the attachment of other cells to the outside, forming an adventitia, or it may become converted into a vein or artery by the addition of the middle and adventitious coats. This is the process by which new vessels are formed in the repair of wounds in granulations, and in other structures which become vascularized.

Angioma Capillare.—This growth forms the simpler kind of congenital *nævus vasculosus* (mother's mark; strawberry mark).

It may be a mere speck, or a considerable "mark," and may increase very rapidly, covering a considerable area, but projecting very slightly above the surface. They are nearly always found in the skin, but may occur also in the subcutaneous cellular tissue or mucous surfaces, and very rarely in internal organs. About two-thirds of the cases occur on the head. The structure consists almost entirely of capillaries, which sometimes have thick walls and many nuclei, sometimes show remarkable dilatations and changes of form, but still preserve the outline of tubes, and do not communicate with each other laterally. Besides these are a little fibrous tissue and some remains of the tissue in which it originates. From the manner in which they spread, there must be, in such nævi, a new formation of capillaries, but the minute process has not been traced. They do not present any capsule or sharp limitation from the surrounding tissue.

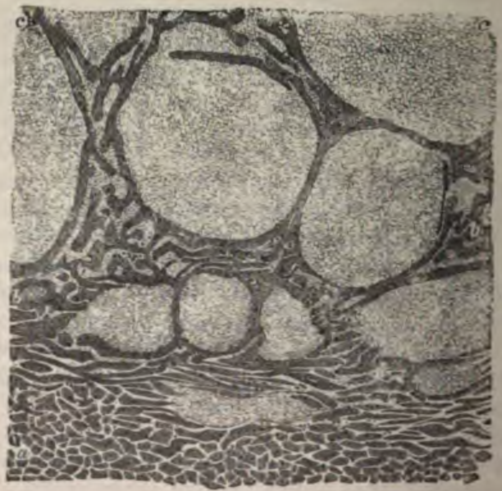
These nævi are nearly, if not quite always, congenital.

There is another form of teleangiectasis which is acquired. It occurs on the skin, in the form of small tufted prominences, composed of a congeries of small vessels, and is usually multiple.

It may follow some inflammation of the skin. I have seen two cases, in one of which the little tufts grew on the scars of smallpox, in another they were said to have followed an attack of scarlatina. Both were on the face.

Angioma Cavernosum.—In this form of bloodvessel tumor the form of tubes is lost, and blood is contained in a number of intercommunicating spaces, which form a structure like that of the corpora cavernosa of the penis. The color of these, when seen externally, is

FIG. 51.



Section of a cavernous angioma of liver.

a, liver-tissue; *b*, reticulated stroma of the tumor; *c*, cavernous spaces filled with coagulated blood.

more purplish and venous than the last. They occur more often in the subcutaneous tissue than in the skin; also in the fatty tissue of the orbit, and occasionally in the pharynx, nose, etc., besides which a special form is found in internal organs. The superficial forms develop in early life; it is said sometimes from the capillary angioma. They often pulsate, and are connected, by wide openings, with arteries and veins, especially the latter.

Cavernous angioma of internal organs is found almost exclusively in the liver. It forms a mass of cavernous tissue, filled with venous blood, not projecting on the surface, and not always clearly marked off from surrounding tissue. The walls of the cavernous spaces are composed of firm fibrous tissue, of the liver-cells entirely absorbed; and the tumor merely replaces a portion of the organ without exerting any pressure on the rest

It is plain from these facts that the affection consists rather in a cavernous metamorphosis of a portion of liver than in a tumor properly so-called. These productions are met with mostly in the livers of elderly persons, and are accompanied by signs of atrophy of the organ, they seldem exceed a walnut in size, and have no clinical importance, being found unexpectedly after death. They may be regarded as formed by a simultaneous atrophy of liver-substance and enlargement of the territory of capillaries, but the order of these changes and their cause are unknown.

I have described (*Trans. Path. Soc.*, xx. 203) a remarkable case in which the liver contained a large number of angiomata up to four inches in diameter, and they were simultaneously present in the suprarenals, ovary, and uterus. The case was so exceptional that no general conclusions as to the structure of these tumors could be drawn from it. Cavernous angiomata are said to have been found, though very rarely, in other internal organs than the liver.

Lymphangioma.—A tumor formed by dilatation of lymphatic vessels. Two kinds are described, corresponding to the two varieties of bloodvessel tumors.

1. Lymphangiectasis.
2. Cavernous lymphangioma.

The two kinds are, however, difficult to distinguish.

1. Lymphangiectasis is a tumor consisting of a mass of dilated lymphatics which usually have a varicose or beaded outline. The shape of tubes is preserved to a great extent, but often the vessels become transformed into irregular cavernous spaces and thus form a transition to the next variety. They are soft, elastic swellings, which when punctured, or sometimes by spontaneous rupture, give exit to lymph. The lining membrane of the cavities treated fresh by nitrate of silver, show the characteristic endothelium of lymphatic vessels. Some are congenital, some acquired. They are often connected with lymphatic glands. The cause of those not congenital is quite unknown.

2. Cavernous lymphangioma. In this variety the form of tubes is lost, and the structure consists of irregular intercommunicating spaces, so as to resemble erectile tissue. The walls of these cavities give the

characteristic silver-staining when examined fresh. Considering that the connective-tissue spaces, or canaliculi, are in direct communication with the lymphatic capilliaries, and form, in Klein's works, their rootlets, it is easy to see that these spaces, as well as the lymphatic vessels proper, may become dilated into lymph-spaces, and the extension of lymphangiomata may be thus partly explained.

These structures sometimes form a diffuse dilatation of lymphatic structure rather than a tumor, as is seen in the congenital condition of *macroglossia* or hypertrophied tongue, where cavernous lymph-structure makes up part of the enlargement.

Macrocheilia, or hypertrophy of the lips, is a similar structure.

The cavernous lymphangioma sometimes occurs in lymphatic glands; sometimes, and perhaps most frequently, in subcutaneous fatty tissue. It has also been occasionally found in the kidney.

In certain forms of Elephantiasis, and especially in the so-called *Lymph-scrotum* (*Varix lymphaticus*, *Nævoid elephantiasis*), great enlargement, and possibly new formation of lymphatics, take place, so as to form large masses, from which a flow of lymph often takes place. But this disease is without doubt caused by a parasite, the Filaria sanguinis hominis, and it has been suggested that all elephantiasis (which is largely lymphatic in structure) may be parasitic. The same parasite causes immense enlargement of internal lymphatics: and the appearances thus produced precisely resemble those of the unexplained lymphangiectases noticed above.

CHAPTER XXI.

SARCOMA.

By this is meant a tumor composed of immature or embryonic connective-tissue; in other words, of that tissue out of which the perfect forms of connective-tissue are developed. It is chiefly made up of cells of different forms, with intercellular substance, or a scanty stroma, which does not, as a rule, form definite spaces, enclosing many cells. It also contains bloodvessels, usually with thin and simple walls. The existence of nerves and lymphatics is not clearly made out.

Sarcoma-tissue is particularly liable to develop into one of the mature forms of connective-tissue—fibrous, cartilaginous, bony, lymphatic, etc.—and hence is often mixed with some one of these tissues. From this fact another definition (that of Virchow) may be framed: "a formation which belongs, in its general features, to the series of connective-tissues, and which differs from the definite species of that series only by the predominant development of cellular elements."

Sarcoma always arises from connective-tissue, in most cases from a connective-tissue organ; but even when it originates in an organ containing epithelium, such as a gland, it is from the fibrous framework, and may be clearly traced to originate by overgrowth or proliferation of the connective-tissue elements. This fact also may be made the basis of a definition—viz.: "Sarcoma is a tumor of connective-tissue origin."

Combining the three criteria above mentioned, we get, as a final definition:

Sarcoma is a new-growth arising from connective-tissue, mainly composed of cells representing an immature condition of that tissue; and if it develop further, reproducing only some connective-tissue type, which is generally, but not always, that of the matrix from which it grew.

Since connective-tissues are developed from the *mesoblast* of the embryo, we might again more simply define sarcoma as a tumor arising from mesoblastic tissues, and if we were always quite sure of the origin of all growths, this might be sufficient. But there are, as will be seen, cases which would make the application of this test difficult.

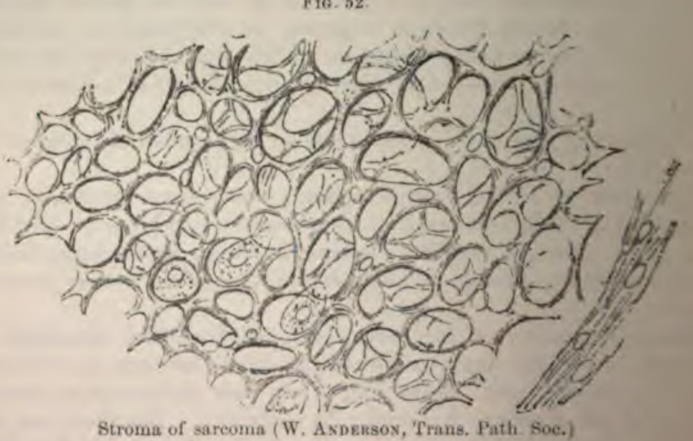
General Characters of Sarcoma.—Sarcoma is more often found in early life than in old age, and mostly occurs between the twentieth and fortieth years. A large number of such tumors appear to be congenital, or nearly so. In other cases there would appear to be an embryonic rudiment which subsequently begins to grow, and shows more complete development.

In early stages the growth appears to be entirely composed of cells; later on there is in many a disposition to form one of the typical varieties of connective-tissue, usually that of the tissue from which the growth springs. Thus sarcoma of bone very often becomes ossified, forming the so-called osteo-sarcoma, or may become cartilaginous—chondrosarcoma. Those from subcutaneous or intermuscular tissue, or fibrous membranes, such as periosteum or dura mater, often become fibrous—fibro-sarcoma. These forms may, however, be sometimes found in tissues of an entirely different character.

At first sarcoma usually forms a distinct tumor separable from the surrounding tissues, which it presses upon or pushes aside without otherwise affecting; sometimes it is enclosed in a capsule. But, as growth goes on, the neighboring tissues may become infected, or changed into sarcoma-tissue, and the capsule, if there be one, is broken through. The direction of growth is generally peripheral—that is, spreading from a centre in all directions. When sarcoma reaches the surface of the body, it may penetrate the skin and grow outward in a form resembling exuberant granulations, or what used to be called fungus medullaris.

The rapidity of growth of sarcoma is in direct proportion to its richness in cells. The cells in rapidly growing forms are usually small, which may be regarded as a consequence of the rapid growth. These forms are generally soft, and hence it may be said, broadly speaking, that a soft sarcoma is more dangerous than a hard.

FIG. 52.



Stroma of sarcoma (W. ANDERSON, Trans. Path. Soc.)

Such tumors are also generally richly supplied with vessels. The bloodvessels may be large, but have very simple walls, chiefly composed of cells. A prolific cell-growth is often seen from the outside of such vessels.

The stroma is usually very scanty, or hardly traceable. Sometimes we can discern a hardened intercellular substance; less frequently we see a sort of framework like that represented in Fig. 52, which surrounds separately every, or almost every, cell. Still more rarely the stroma forms distinct alveoli enclosing several cells. This "alveolar sarcoma" will be spoken of as a distinct variety.

Degeneration of Sarcoma.—Besides the different modes of productive growth, sarcoma may become altered by degeneration.

Softening is the commonest form, and is caused by mucous degeneration. This sometimes gives rise to cysts. Ulceration may occur on the surface, but affects the tumor only, and does not give rise to destructive spreading ulceration of surrounding parts, as in carcinoma.

Various kinds of sarcomata are distinguished:

1. Small round-celled sarcoma.
2. Large round-celled.
3. Spindle-celled.
4. Giant-celled, or myeloid.

Besides these we may have mixed forms, or combinations of the above, and also certain rarer forms, viz.:

Alveolar sarcoma.
Melanotic sarcoma.
Plexiform sarcoma, or cylindroma.
Glioma or gliosarcoma.
Psammoma.

Also combinations with other tissues; as fibro-sarcoma, chrondro-sarcoma, osteo-sarcoma, myxo-sarcoma.

Small round-celled Sarcoma.—The cells are not, as a rule, larger than lymph-corpuscles, and have a great resemblance to them. The real difference is, however, that they have a large round or oval nucleus, usually granular, with a small amount of protoplasm around it, while in lymph-cells the nuclei are smaller and often multiple.

This kind of tumor is usually soft, whitish and "medullary," or like marrow in appearance. There is little or no fibrous tissue, and little stroma of any kind between the cells. It usually grows fast, and is apt to be very malignant in its properties, readily invading neighboring tissues and forming metastases to distant parts. Many such growths would formerly have been called "soft encephaloid cancer." They differ from cancer as structurally defined, in not having the cells contained in spaces with an alveolar stroma and in the cells being roundish and simple, not of the epithelial type.

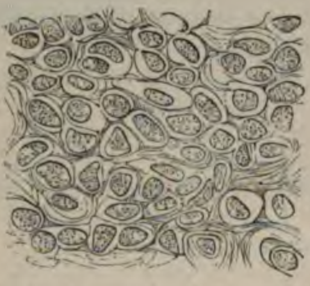
Lympho-sarcoma is usually spoken of as a variety of small-celled sarcoma. By this is meant a tumor composed of small lymphoid cells, held together by a reticulum such as is described in speaking of lymphoma. Most of the growths thus described are here arranged under the head of lymphoma with malignant properties. But it is extremely difficult to draw the line between that tumor and lympho-sarcoma. As a rule, it may be said that, when the cells agree entirely with lymph-corpuscles in size and character, there is no reason to call the growth sarcoma.

Small round-celled sarcoma originates from many parts where there is connective-tissue, especially from periosteum and fibrous membranes, fasciæ, etc., and may undoubtedly originate in lymphatic glands.

Secondary growths of true sarcoma occur most frequently in the lungs, but also in other parts. The metastasis may take place through the veins, or through the lymphatics, most commonly through the former.

Large round-celled Sarcoma.—In this the cells are larger but do not differ in size alone from the last-mentioned variety. The cells are often various in form and magnitude. They have a distinct protoplasm, with large round or oval nuclei, often containing brilliant nucleoli. There is often an intercellular stroma, which surrounds each cell individually, or encloses at most two or three in one space. Signs of cell-division are often seen.

FIG. 53.



Section of a secondary, large, round-celled sarcoma of the lung.

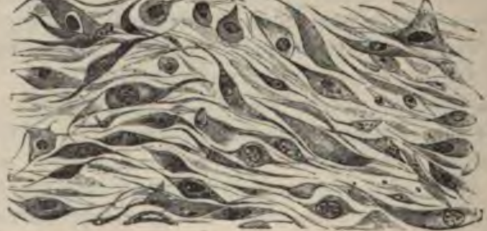
Cells varying in shape, closely pressed together, with scanty fibrous stroma. The nuclei are large and very deeply stained (carmine-staining. 400 diameters).

This variety is firmer, and grows, as a rule, less rapidly than the last; it agrees in its clinical characters with spindle-celled sarcoma. The cells have also much resemblance to spindle-cells in their characters, except in outer form.

Secondary growth from an originally spindle-celled sarcoma, is often, as in the specimen figured, of this kind.

Spindle-celled Sarcoma.—The cells in this variety are elongated and drawn out at each end into a point so as to be awn-shaped, or what are called spindle-cells. There is usually one distinct oval nucleus, with brilliant nucleolus. Two nuclei may be seen in cases where rapid cell-growth is going on. There is little or no intercellular substance and no proper stroma. The bloodvessels are wide and have cellular walls.

FIG. 54.



Sarcoma composed of large spindle-cells with distinct nuclei often containing nucleoli. (400 diameters.)

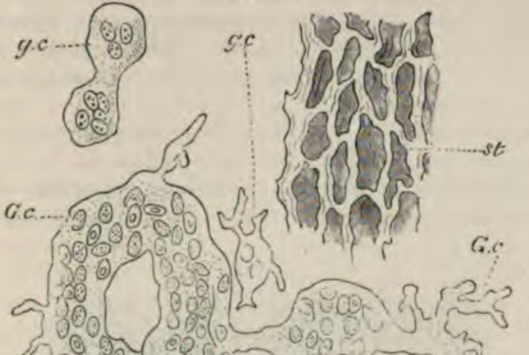
These cells are arranged in a parallel order, so as to form bundles, which are either themselves parallel, or twisted and interlaced. If the latter, a section will show some bundles cut across, and the cells will in those parts appear oval or round. Cells with more than two processes, or stellate, are sometimes met with. The structure much resembles connective-tissue in process of formation from granulations, and hence these growths have been called fibro-plastic tumors.

The small-celled and large-celled forms have been described by some authors as distinct varieties, but the difference, except in size of cells, is not well-marked. Their consistence is usually firmer than in the case of round-celled sarcoma; and it is only rarely, when degeneration occurs, that they have the appearance called medullary.

Situation.—Spindle-celled sarcoma grows from various forms of connective-tissue, especially fasciæ, intermuscular septa, subcutaneous or submucous tissue, periosteum, etc., sometimes, also, from the fibrous tissue of the glands, as the mamma, and more rarely in internal organs.

Clinical Characters.—At first these tumors affect neighboring parts only by pressure, as they are generally distinct and have not much tendency to infiltrate. If removed they frequently recur, and in many cases give rise to secondary tumors, the metastasis taking place either by the veins, to the lungs, or through the lymphatic system. They must therefore be regarded as malignant; but this character is, for obvious reasons, more marked when they occur in internal organs than in the limbs or surface, where removal is possible.

FIG. 55.



Unusually large multinucleated giant-cells and simple cells of myeloid sarcoma (after BRISTOWE).

c c, simple cells with one or two nuclei; *g c*, giant-cells; *s t*, portion of stroma.

Giant-celled or Myeloid Sarcoma.—This variety is known by containing large multinucleated cells. These are called myeloid from the Greek word for marrow, because similar cells are met with in the marrow of the bone, and sometimes in periosteum. They are flat protoplasmic masses of irregular shape, containing several oval nuclei, in some cases even as many as fifty. Whether they are identical with the "giant-cells" of tubercle and other new-growths is doubtful. Cells of other forms, chiefly spindle-shaped, make up the great mass of the tumor.

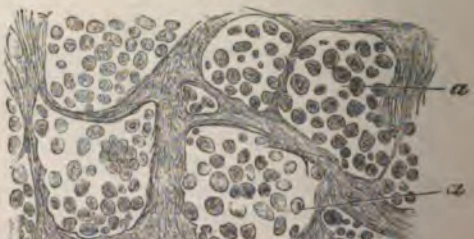
Giant-celled sarcoma generally, if not always, originates in bone, either centrally or from the periosteum—*i. e.*, in situations where the myeloid cells are normally found. The physiological function of these large multinucleated masses appears to be connected with the removal of calcareous matter, and thus hollowing out or altering the shape of the bone. Kölliker observed similar cells (to which he gave the name osteoclasts) on the surface of bone in various situations where absorption was taking place—for instance, on the surface of fragments of dead bone. Another situation for "osteoclasts" is in the periosteum of the lower jaw. This bone is known to undergo in old age a change, which consists in the ramus becoming less vertical; a change which can only take place by the gradual removal of bone from one part, and perhaps deposition in another, and is, according to Kölliker, effected by the osteoclasts.

Again, the medullary cavity of long bones, whether the hollow of the shaft or the cancellous structure of the ends, is formed by the gradual hollowing out of what was originally a solid rod of cartilage. Now these two situations are among the typical seats of myeloid sarcoma. On the jaws this tumor is one form of the growths which are clinically grouped together as "epulis." It must not be supposed that the giant cells necessarily exercise in new-growths the functions which belong to them physiologically. But these facts illustrate the general law that tumors reproduce the physiological type of the tissue from which they spring

Myeloid sarcoma is, on the whole, less malignant than other forms of sarcoma, but metastases do sometimes occur.

Special Varieties of Sarcoma—Alveolar Sarcoma.—In this rare form of growth the cells are arranged in alveoli divided by fibrous

FIG. 56.



Alveolar sarcoma, secondary tumor, derived from a primary tumor of bone. *a a*, groups of cells with intercellular substance contained in alveoli.

septa, so as to have a great resemblance to cancer; and when this structure was taken as the criterion of cancer these growths were called by that name. It is not always easy to distinguish this tumor from cancer. Generally, the following characters make the distinction:

1. The cells are roundish and simple, not of an epithelial type.
2. There is generally some homogeneous intercellular substance, or else a sort of stroma passing inward from the fibrous septa, and enclosing each cell. This feature, if it be present, is decisive.
3. The growth originates in some form of connective tissue.

These distinctions will be enough, except in certain very rare cases of transposition of tissues during embryonic life.

Pigmentary or Melanotic Sarcoma.—In this the cells, which are either spindle-shaped, round, or irregular in form, contain pigment. This is no accidental feature, since it may be traced through the whole of a tumor, and even in secondary growths derived from it. The color of the tumor is thus brownish, mottled, or nearly black. Less commonly pigment is found in the fibrous septa, as well as in the cells.

Melanotic sarcoma almost always begins in some organ normally containing pigment, such as the skin, the eye, or the pia mater. Exceptions to this rule are very rare. Sometimes the growth begins in a congenital pigmented mole or wart on the skin. This is a decidedly malignant growth—more so, speaking generally, than the corresponding form without pigment.

Plexiform Sarcoma or Cylindroma.—The name Cylindroma has been applied in at least two different senses:

1. To a tumor in which sarcoma-tissue is mingled with that of myxoma, and in which the former is regarded as having undergone mucous degeneration. This may also be called myxo-sarcoma or sarcoma myxo-matodes.
2. Generally a more distinct kind of growth is implied by the name—one in which bloodvessels are seen invested by a hyaline or mucous sheath, which has in parts an investment of cells. Here it is thought that the adventitia of the vessels has undergone mucous swelling and degeneration.

Most observers have regarded the original tissue as sarcoma, some as angioma. The same growth appears to have been described, by Moxon, as peri-angioma.

Most of such tumors have been found in the brain. They are rare; and the subject requires further elucidation.

Glioma.—Under this name are comprised two kinds of growth which, though similar in structure, are very different in clinical features:

1. *Glioma of the brain and spinal cord.*
2. *Glioma of the retina.*

The former is a strictly local growth, which may be considered as a mere overgrowth of the neuroglia of the nerve-centres (*see* page 207). The second, though simple in structure, is generally infective to the neighboring structures, and has, in rare instances, given rise to secondary growths in distant parts. It is, therefore, malignant, and seems rightly classified as a form of sarcoma.

Glioma of the Retina.—This forms a special growth, only occurring in childhood and sometimes congenital, which gives a peculiar metallic lustre to the fundus of the eye. It was formerly known as encephaloid or pseudo encephaloid.

The structure is like that of the granular layers of the retina, consisting of a fibrillar basis-substance with round nuclei. and this closely resembles that of cerebral glioma. That of the retina has, however, very different properties, being of comparatively rapid growth, locally infective, and often highly malignant. Various structures of the eye and the orbit may be successively affected: and, in very rare instances, metastases in internal organs have been observed.

Retinal glioma often passes into sarcomatous structure, and has the clinical characters of sarcoma. The malignancy, even of the pure forms, is well marked.

For a minute description we must refer to works on ophthalmic surgery.

Psammoma.—Small globular masses, composed of concentrically arranged cells, usually flat, are sometimes found attached to the choroid plexus, or on other parts of the investments of the brain. They seldom exceed a small pea in size. The central part is often calcified, and under the microscope, if treated with dilute acid, may be seen to evolve bubbles of carbonic acid. Hence the name psammoma or sandy tumor.

Some of these tumors may be fibrous, but generally the cells composing them are derived from the endothelium. Since this is generally regarded as a form of connective-tissue, they are now classified under the head of sarcoma, but have little resemblance to the other forms. Their growth is limited; they have no malignant properties, and are of no clinical importance, except in the rare cases where they are large enough to exert some pressure.

Endothelioma is a name sometimes given to this and other growths originating in, and composed of endothelium. The name is also applied to sarcoma with alveolar structure, where the cells contained in the alveoli resemble, and are derived from, endothelia.

If the endothelium of the serous membranes lining the great cavities of the body be regarded, in accordance with modern embryological views, as derived from the hypoblastic epithelium, the distinction intended by the word endothelioma becomes unimportant.

CHAPTER XXII.

NEW-GROWTHS OF EPITHELIUM—CANCERS.

OVERGROWTHS of epithelium (including together the epiblastic and hypoblastic tissues) may be, like mesoblastic growths, either typical—*i. e.*, hyperplastic, or atypical. If we classify them according to the different varieties of epithelium found in the body—viz., (1) Pavement or flat-celled, and (2) cylindrical or columnar-celled, including, as a variety of the latter, (3) the so-called spheroidal glandular epithelium—we find that each of these varieties may give rise to both typical and atypical growths. There is thus no epithelial growth which has to the rest the relation which sarcoma bears to connective-tissue tumors, as being their immature or embryonic stage. The atypical or irregular growths arising from all kinds of epithelium are, however, called by one name, viz., cancer or carcinoma. We have thus two main kinds of cancer—(1) squamous-celled, generally known in this country as epithelioma, or epithelial cancer; (2) glandular cancer, including those derived from both columnar and spheroidal epithelium, between which no clear distinction can be drawn.

It will be practically most convenient to take the simple typical growths first, and then the cancers.

I. **Typical Growths from Squamous Epithelium.**—Such growths from the pavement epithelium of mucous surfaces are hardly known, since the *polypi* of these surfaces are more complex structures. From the epidermis, which is a variety of squamous epithelium, they are commoner.

Outgrowths of epidermis alone form the structures called horns of the skin (*cornu cutaneum*), which may attain a length of several inches. Specimens are to be found in most pathological museums. Their cause is unknown.

Commoner epidermic growths are warts, including the so-called simple warts, pigmented warts, etc.

Another class of tumors, chiefly epidermic in structure, is *molluscum contagiosum*. In the latter case, however, it is pretty clear that the growth is caused by some specific irritant, possibly a parasite, though its nature is not absolutely determined. A similar specific cause, it may be remarked, is not impossible in the case of the "common wart," and, on some grounds, even probable.

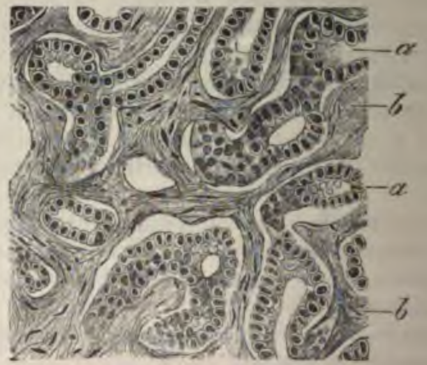
In these cases the growth of epidermis is chiefly outward, and is mostly due to hypertrophy of the papillæ.

Sometimes, on the other hand, there is a growth inward of the interpapillary processes, though to no great depth. The columns of epidermic cells, in such a case, sometimes form concentric masses, of which the inner cells undergo the horny degeneration characteristic of epidermis, so as to appear homogeneous. These bodies are called "pearls," or "birds'-nests." They are few and unimportant in simple epidermic tumors, but have a characteristic importance in cancer of the skin.

The essential character of all the above growths is that the normal boundary between epidermis and dermis is preserved. They are called by most French and some German writers epithelioma, a name corresponding to fibroma, chondroma, etc., but this name is usually reserved in this country for malignant growths of squamous epithelium or epithelial cancer.

Simple Glandular Tumors or Adenomata.—Various acinous secreting glands may give rise to tumors by simple overgrowths. Such tumors are not uncommon in the skin, arising from the sweat-glands or the sebaceous glands, and are called Adenoma sudoriparum and A. sebaceum respectively. Sebaceous tumors are sometimes combined with a collection of sebaceous matter, called an atheromatous cyst, but the latter may occur without a tumor properly so called. Tumors of the skin-glands may become calcified or even truly ossified. Adenoma of the mamma constitutes the chronic mammary tumor or Adenocele, well known to surgeons. Adenoma of mucous glands occurs in the nose, the pharynx, the ear, etc., and constitutes one form of so-called mucous polypi sometimes termed adenoid vegetations.

FIG. 57.



Primary adenoma of liver.

a, tubular gland structure; *b*, fibrous stroma.

Adenoma of the kidneys, liver, and other glands, is also met with. One form which arises primarily in the liver is of great interest, as differing in structure from the hepatic cells. Whether it takes its origin in the bile-ducts, or in a fragment of the primitive intestine, accidentally included in the course of development, must be regarded as uncertain. Such growths have, in one or two instances, given rise to secondary tumors—for instance, in the kidney, as seen in the specimen previously figured (see Fig. 40).

Adenoma of glands with marked cylindrical epithelium, such as that of gastric and intestinal glands, has sometimes been called cylindrical or tubular epithelioma, and the use of this name has given rise to some confusion. Such tumors, when simple and circumscribed, are, strictly speaking, adenomata. They seem, however, to be rather liable to pass into carcinoma—that is, a tumor originally glandular becomes carcinomatous—and hence they have often been regarded as a distinct class. The malignant forms are cancers. In the rectum new-growths are found, of glandular structure, like Lieberkühn's crypts, and presenting every transition from an innocent tumor up to pronounced cancer (Cripps).

A well-marked form of adenoma occurs in the ovary, where it is associated with, and is thought to be the origin of, the large cystic tumors of that organ; the follicular epithelium developing into acinous glandular structure, which becomes cystic.

The *ductless glands* may also develop similar tumors, bearing the same relation to the epithelium of other closed follicles as the other adenomata do to the secreting epithelium. Chronic swelling of the thyroid, or bronchocele, may be thus regarded in its early stage. In a few very extraordinary cases, tumor composed of thyroid tissue has been observed in other parts of the body as a secondary growth (*Trans. Path. Soc.*, xxxiii. 291). The secondary growths have always been found in bone.

II. **Atypical or Malignant Epithelial Tumors, Cancers, or Carcinomata.**—The term cancer, which was formerly used in a clinical or physiological sense to signify tumors having the properties called malignant, is now a structural or anatomical term, meaning tumors starting from epithelial tissues, and composed of epithelial cells irregularly arranged, not forming a uniform layer like epidermis, nor a typical gland-structure. This irregularity mostly depends upon the epithelial cells not being confined within their normal boundries, but invading the connective tissue. This invasion, or, as it is called, infection of the connective tissue, is a feature characteristic of malignancy, since, as above explained, all the properties called malignant may be deduced from it.

It would follow that all atypical epithelial tumors or cancers are malignant, and this is generally, if not quite universally, true; but it may be well to reiterate that the converse is not true, *i. e.*, all malignant tumors are not cancers, since many sarcomas and lymphomas are equally malignant.

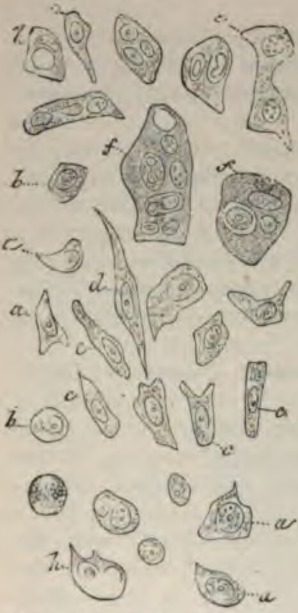
Since cancer is epithelium out of its place or growing in a foreign tissue, it is more complex than sarcoma, and we have two parts to consider; (1) the *cells*, (2) the containing-tissue, called the *stroma*.

1. The **cells** are epithelial cells derived from the epithelium of the part, either by continuous growth, or, in the case of secondary tumors, from "something" transported to a distance. This "something" is probably in all cases a portion of the original tumor, *i. e.*, a cell or cells forming a graft or bud of the original stock. It has been supposed that something different from cells is what is thus transmitted;

either in an infective juice or some minute particles like seeds of cells—a *seminium*—which exerts a peculiar influence on the cells of the distant part, causing them to grow in the likeness of the original tumor. But no evidence has ever been given of the existence of any such substance, and the theory of transplantation of cells, which rests on positive facts, is therefore more reasonable.

If this be true, all the cells of the original cancer, as well as of the secondary growths, must be direct descendants of the epithelium of the part, just as the cells of the mature body are of those of the embryo.

FIG. 58.



Various forms of cancer-cells. (CORNIL and RANVIER).

a, angular or battledore-shaped; *b*, spherical; *c*, composed of prismatic; *d*, spindle-shaped; *e*, hour-glass-shaped; *f*, *h*, cells showing mucous degeneration.

The cells of cancer, primary or secondary, preserve in their after-development most of the characters of the tissue in which they originated. The only exceptions to this rule are that in large and rapidly growing secondary tumors the characters are sometimes not well marked; and when growth is rapid the cells are irregular and often contain more nuclei than one; and that they are often altered in shape by mutual pressure.

Thus when cancer of the breast produces growths of the axillary glands, we find in the midst of the lymphatic gland epithelium like that of the mammary gland. When glandular cancer of the duodenum or the rectum gives rise to secondary cancer of the liver, we find, in the latter, structures like Lieberkühnian glands. In fact, there is bowel-tissue in the liver, and so in many other cases.

2. The Stroma of Cancer.—The stroma is essentially the tissue of the part into which the epithelial growth extends. It is connective-tissue, either normal or hyperæmic, or inflamed and filled with leucocytes or nuclei. The connective-tissue may also undergo hyperplasia according to the ordinary process, and thus a good deal of it may be of new formation. But it is not formed out of the epithelium, which only acts as a sort of irritant, stirring up growth. The cells of the stroma are accordingly distinct from those enclosed in the alveoli, and present the general characters of connective-tissue cells, as will be seen in Figs. 62 and 64.

The stroma carries the bloodvessels of cancer, and these do not penetrate the cell masses.

It is usually arranged in irregular spaces freely communicating with one another, which look roundish or oval on section, called *alveoli*. This alveolar structure is, in the main, characteristic of cancer, being found in all forms, though less developed in epithelioma, and being only seen in rather rare forms of sarcoma (alveolar sarcoma).

The stroma, like the cells, is subject to degeneration, especially fatty; and may be, in rare cases, calcified.

Cancers, like simple epithelial growths, form two great groups:

1. Squamous-celled or epithelial cancer, or what is usually called epithelioma.

2. Glandular cancer, including those derived from cylindrical or tubular glands, and from spheroidal epithelium, which forms histologists now generally comprise in one class.

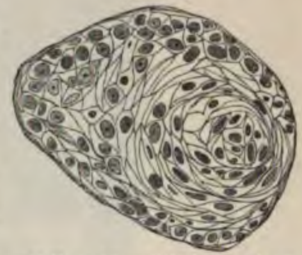
Cylindrical epithelium of surfaces (*e. g.*, the respiratory tract) does not appear to give rise to cancer. One does not quite see why it should not do so, and possibly instances of this formation may hereafter be discovered; but up to the present time it would appear to be the rule that cancers of such surfaces always originate in their glands.

In the case of the intestinal epithelium, however, the cylindrical cells of the surface are so much like the cells of the tubular glands that it is sometimes very difficult to say whether any particular tumor is to be regarded as having originated from surface epithelium or from glandular epithelium.

Flat-celled Epithelial Cancer—Epithelioma.—This form may be found wherever there is squamous epithelium or epidermis. Its favorite seats are the skin, especially of the face; and the genitals, mucous surfaces adjacent to the skin, as those of the mouth, the ear; also in the pharynx and œsophagus, the vagina and cervix uteri, etc.

The tumors may project on the surface in the form of a wart, or may form hard flat masses, or a diffuse infiltration. On scraping the surface of a cut section, squamous cells are obtained, both loose and in the form of concentric bodies called globes, pearls, or cell-nests (Fig. 59). By pressure whitish plugs may be squeezed out, which consist of masses of the same cells.

FIG 59.



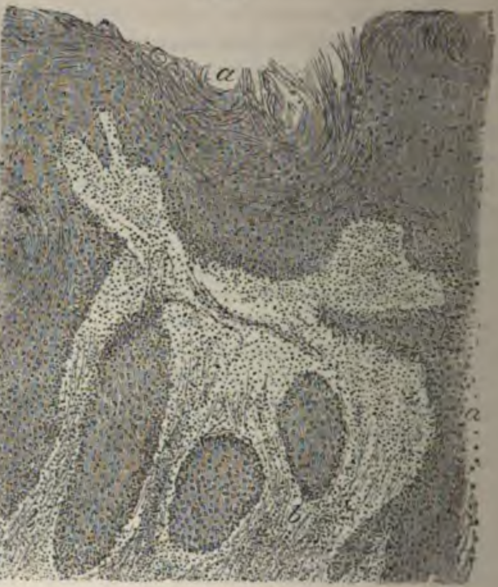
Cell-nest in epithelioma showing the concentric structure and angular forms of the cells produced by mutual pressure.

The tumor is formed by an increase and inward growth of the epithelium or epidermis, which penetrates the subjacent corium or connective-tissue in columns of cells, which though, in cross section, they may exhibit apparently isolated masses, are all in connection with the original mass (Fig. 60).

In these masses the concentric cell-nests may be seen abundantly, and in the case of skin-cancers the central part often undergoes a horny degeneration like that of the superficial layers of epidermis. It is evident that in its relation to the blood supply the centre of the globe corresponds to the surface of the epidermis. The degeneration does not occur uniformly but at intervals. Such globes are occasionally found in simple epithelial growths, but less abundantly than cancer.

The stroma of the cancer is formed by the connective-tissue of part. This may be little changed, but may be more vascular; or fibrous bundles may be hypertrophied; or the tissue may be infiltra with leucocytes; or may be merely more abundantly supplied th usual with nuclei. These changes must be regarded as inflammato and caused by the irritation of the epithelial growth. This irritati may, of course, as in other cases, lead to a new formation of conne

FIG. 60.



Squamous-celled epithelioma.

a, superficial horny epidermis penetrating into the corium; *b*, nucleated connecti tissue of the corium.

tive-tissue, and hence part of the stroma may, as well as the epith lial cells, be a new-growth. However abundant the small-cell infiltration of the stroma may be, we never see transitional form between these small cells and the epithelial cells.

In some cases it is very difficult to say whether the origin of growth was from the epidermis or from the skin-glands, especially sebaceous glands (which, embryologically, are derived from an invo tion of the epidermis), or again from the sheaths of hair.

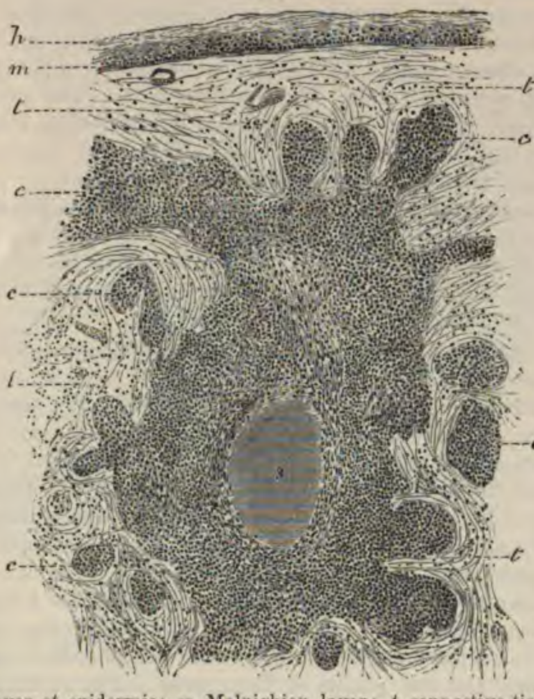
Epithelioma is more especially a disease of advanced life, thou these cases occur, exceptionally, in young persons. It is probable th the wasting of connective-tissue in older individuals, by opposing resistance to the growth of epithelium, favors the growth of this fo of cancer.

The growth of epithelioma is often very slow. It is very liable to ulceration, and by this process causes great destruction of the tissues. In these respects great differences are seen, according to the situation of the cancer. It spreads, in the first instance, to the neighboring lymph-glands, and comparatively rarely gives rise to secondary growths in distant parts.

The consideration of the clinical characters and other features in the growth of epithelioma belongs to works on surgery.

Rodent Ulcer.—This is a form of malignant cutaneous tumor regarded by English surgeons, though not by most Continental writers, as distinct from the flat-celled epithelioma just described. This histological difference between the two forms is that in that now spoken of the cells are much smaller, not squamous in form, and do not undergo horny degeneration, so that cell-nests or pearls are rarely if ever met with.

FIG. 61.



h, horny layer of epidermis; *m*, Malpighian layer; *t*, connective-tissue of corium, with abundant nuclei; *c*, masses of new epithelial cell-growth, starting from the outer root-sheath of hair.

The cells are contained in distinct alveoli, which cannot generally be traced to be continuous with the surface epidermis. On all these grounds it seems that the origin must be different from that of flat-celled epithelioma, and cannot be referred to the epidermis as a whole. The normal elements most like cells of rodent ulcer are those of the deepest part of the Malpighian layer, the external root-sheath of hairs, and, to a certain extent, the epithelium of sebaceous and sudoriparous glands. Now the origin of all these appendages of the skin is the same.

They are all formed by an ingrowth of the deepest portion of the Malpighian layer during fœtal life. Although we cannot distinguish those cells of the fœtal epidermis which are destined to form the cutaneous appendages, from those which are destined to form the superficial horny epidermis, there must be some original difference between them which makes them develop in a different way, and possibly the one set may originally be more deeply seated than the other.

At all events, as new growth sometimes indicates an original developmental distinction not otherwise traceable in the adult body, we may say that squamous epithelioma arises from that portion of epidermis which is endowed with the power of forming superficial horny scales; while rodent ulcer originates in that portion which either has formed or is capable of forming the appendages of the skin.

Very different views have been taken of the origin of rodent ulcer by different observers, and by the same observer at different times, it having been referred to the sebaceous or to the sweat glands, to the sheaths of hairs, or to the deepest part of the Malpighian layer.

None of these modes of origin is impossible, and I believe that, in fact, each may have been true of particular specimens.

Fig. 61 represents the commonest appearance in specimens of rodent ulcer, where the small-celled growth is seen to start from the external root-sheath of a hair, and grow out in prolongations into the surrounding tissue, while small masses of the cancer, cut in section, present the appearance of the alveoli.

Another specimen, which has more the appearance of a glandular tumor, is described and figured below.

Gland-cancer.—Various kinds of glands may give rise to cancer. The ultimate structure is much the same in all, but in some the glandular arrangement of the epithelium in follicles or acini is preserved much longer than in others. These are differences of degree; but still there is a convenience in following the old distinction, now neglected by histologists, between glands with spheroidal and those with columnar epithelium. To the former belong the glands of the skin, and the mammary gland (which may be regarded as a highly-developed sebaceous gland), the others, called special-secreting glands, and the kidney. To the second belong most of the glands of the stomach and intestines, and the glands of the uterus. The epithelium of the Graafian follicles of the ovary, and that of the closed follicles of the thyroid, supra-renals, and the remaining blood-glands, form a third class.

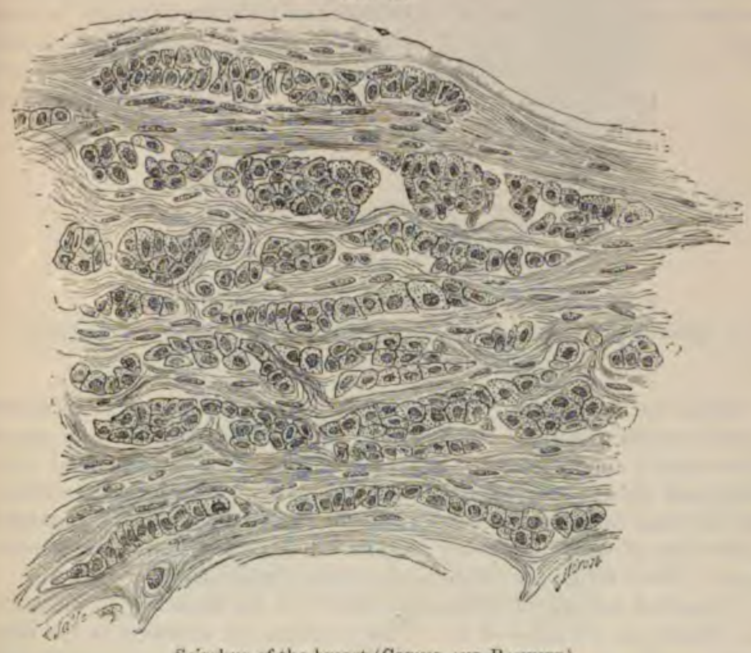
Glands with spheroidal epithelium, when they form cancer, soon lose the acinous or glandular arrangement, and present the alveolar structure of cancer. The glandular origin being thus obscured, these forms are sometimes known as carcinoma vulgare or simple cancer. Mammary cancer is the best type.

Cylindrical-celled glands often grow into large masses, indistinguishable from simple adenoma before the structure breaks up into the irregular form of cancer. Hence, these have been called adenoid cancer or tubular epithelioma. Malignant growths arising from the Lieberkühnian crypts of the duodenum or the rectum (rectal cancer) form the best type. These are often with difficulty distinguished from simple adenoma of those parts.

Without further attempt at classification it will be most convenient to take in order the different organs which cancer most commonly affects.

Cancer of the Mamma.—This, the most carefully studied of all cancers, is found in masses which present perfect alveolar structure, and thus have been called carcinoma simplex. The cells are multiform and angular by mutual pressure, but, when they have room to grow, resemble spheroidal epithelium, containing one or more large nuclei. Larger and more complex forms are sometimes seen. They have a marked tendency to fatty degeneration, which may be compared to the fatty metabolism by which milk is produced in the normal epithelium of the gland. The stroma is various in amount and character, presenting all the varieties above spoken of. When this is very abundant and hard the *scirrhus* form is produced. In this the cells undergo atrophy, and the tumor wastes and shrivels while continuing to grow at the margins.

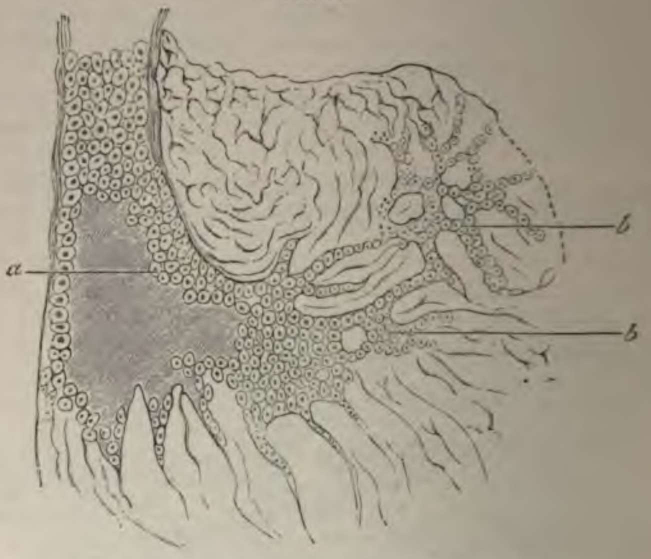
FIG. 62.



Scirrhus of the breast (CORNIL AND RANVIER).

The fibrous tissue, contracting like a scar, also contributes to the atrophic process. The growth is slow.

FIG. 63.



Mammary cancer infecting the connective tissue (WALDEYER).
a, epithelial proliferation, starting from a mammary acinus; *b b*, epithelial cells passing into the connective-tissue spaces.

When the cells are very abundant and the stroma scanty, the cancer is often called medullary, being much softer in consistence. It grows more rapidly than scirrhus. This form is very liable to central softening and decay, large masses of degenerated tissue being produced. But no clear line can be drawn (unless cicatricial atrophy be regarded as the sign of scirrhus), many tumors having an intermediate consistency. Both forms are liable to destructive ulceration.

A marked feature of mammary cancer is its tendency to infiltrate the tissues on all sides of it. This explains its adhesion to the skin above, and to the muscles and ribs below. By the same process cell-columns insinuate themselves into the connective-tissue spaces and thus into the lymphatics, the axillary lymph-glands being first affected. After this the pleura and lungs may become infected, and secondary tumors may be formed in distant parts.

Colloid cancer, showing the peculiar degeneration of the cells, sometimes occurs. Mammary cancers are classified in a different manner by some surgeons, as *acinous* and *tubular* (Billroth).

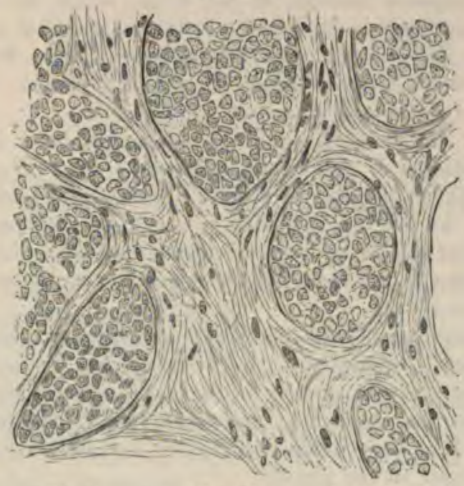
Although, as a rule, no glandular structure is seen in mature mammary cancer, especially in the marginal parts, which are generally examined, minute investigation has shown that in many cases certainly, and probably in most, it starts with a morbid growth of the acini of the gland.

There is, however, a distinct though rare form called "Duct Cancer," in which the morbid growth appears to start from the epithelium of the mammary ducts. In this form the alveolar groups of cells, even when of a considerable size, exhibit a central lumen and columnar epithelium arranged in a typical manner around it. It is a rare variety of cancer, and I have myself had the opportunity of examining one specimen only.

The infiltrating and infective mode of growth distinguishes it from an adenoma.

Cancer of the Skin-glands.—The sebaceous and sudoriparous glands show much more tendency to form simple adenomata than cancer. Nevertheless, true cancers may be developed from them, producing some of the tumors known to surgeons as rodent ulcer. An example, probably starting in the sebaceous glands, from the cheek of a young woman aged 27, is given in Fig. 64. It might almost be taken for scirrhus of the breast.

Fig. 64.



Gland-cancer of the skin, or rodent ulcer.

This form is usually seen in the upper part of the face. It is much less malignant than mammary cancer. The growth is generally slow, and the growth remains local for an indefinite period. The lymphatic glands are rarely affected; but this exemption is perhaps due to locality, since other morbid processes affecting the same parts (lupus, and ordinary suppuration, as impetigo contagiosa) rarely affect the glands. The lymphatic communications of this part of the skin appear to be scanty. When destructive ulceration is once established, it is extremely formidable, and may be rapid. It is by no means certain that all cases of "rodent ulcer" are of this nature.

Cancer of the Stomach.—It is probable that all stomach cancers originate in the gastric glands, and therefore follow the general law of glandular development. It is a remarkable fact that simple adenoma of the stomach is almost unknown: a glandular growth, however arising, appears generally to become malignant.

The form which has most resemblance to simple adenoma is that which is called *malignant adenoma* or adeno-carcinoma (Ziegler), also called columnar epithelioma, which is, however, a very rare form of disease.

In this the gastric glands at a special part of the surface appear to enlarge, forming tubular glands much larger than the normal, lined with a tall cylindrical epithelium, while the other structures waste and disappear. The same glandular structure extends downward, affecting all parts of the stomach-wall in turn, till it is converted into a nodular tumor, which simultaneously extends in a lateral direction.

The general structure, in this stage, is not that of alveolar cancer, but consists of a mass of interwoven tubular glands, with marginal epithelium. The tumors are soft and liable to ulceration. They are highly malignant, often producing secondary growths in the lymphatic glands and metastatic nodules in the liver; while in rare cases secondary growths have been found in various organs, even the skin (*Trans. Path. Soc.*, xxxiv. p. 102, Plates 8, 9). The secondary growths have more the character of ordinary cancer, but still may preserve the tubular gland-structure.

We may say that this character of malignancy belongs to most columnar gland-tumors of the whole intestinal tract. Why this should be the case in these organs, while gland-tumors of the skin are rarely malignant, we do not know. But possibly the higher temperature and rich vascular supply of internal organs have something to do with it; since Roy has shown that high temperature produces relaxation of the tissues generally.

The more ordinary forms of cancer of the stomach are generally distinguished as, 1. Medullary; 2. Scirrhus; 3. Colloid.

1. Medullary or soft cancer forms large masses of new-growths, chiefly at the cardiac extremity, and often round the cardiac orifice of the stomach. It is very liable to softening and ulceration. It is said always to originate in the glands.

2. Scirrhus or hard cancer differs not only in the degree of hardness but in its situation, being found at the pylorus or near the pyloric extremity.

The abundance of fibrous tissue in cancers of this part is clearly due to the abundance of fibrous and muscular tissue in the walls of that end of the stomach. The structure is essentially the same as that of the other variety, but masses are sometimes met with, composed chiefly, or it would seem wholly, of fibrous tissue. Hence they are described as fibrous induration of the pylorus. The writer has seen specimens in which no cells could be discovered in the part examined. The probability is that such a mass is the scar of cancer.

3. Colloid cancer occurs, though rarely, sometimes combined with

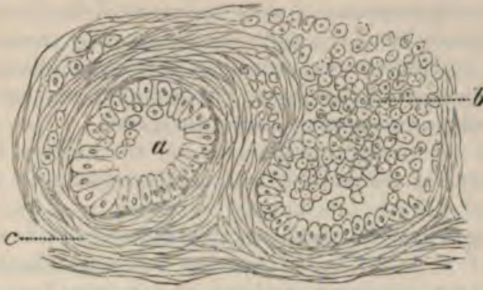
simple cancer, sometimes alone. Even the earliest stage shows the characteristic structure.

All the above may extend in the usual ways of cancerous tumors: (1) by direct contiguity to the liver, and other adjacent organs; (2) by lymphatics to the retro-peritoneal glands; (3) by embolism of the portal vein to the liver; (4) to distant organs, probably by the blood-circulation.

Cancer of the Intestines.—This presents the same types as in the stomach.

Malignant adenoma ("columnar epithelioma") has been found in the duodenum, but more frequently in the large intestine, especially in the rectum, where it forms the typical rectal cancer, which is the commonest form of intestinal cancer.

FIG. 65.



Primary malignant adenoma of duodenum (DR. S. COUPLAND, Trans. Path. Soc., xxiv., pl. iii.).

a, gland-tubule with columnar epithelium, which shows commencing proliferation with production of smaller and irregular cells; *b*, another tubule showing cell-proliferation in a more advanced stage; *c*, connective-tissue stroma.

The transition from the glandular type of growth to the atypical arrangement of cancer may sometimes be traced, as in the specimen figured (Fig. 65), which is that of a primary malignant adenoma or cancer of the duodenum. It affected the gall-bladder, and produced also one secondary nodule on the liver, which later was carcinomatous but not glandular in structure.

The ordinary cancer, in its medullary and scirrhous varieties, also occurs, and has been in some cases traced to its origin in the Lieberkühnian glands. It causes constriction. Well-marked scirrhus is not common. Colloid, on the other hand, is more often met with here than in the stomach, and is often combined with the same disease of the peritoneum.

Intestinal cancer gives rise to secondary growths precisely in the same manner as cancer of the stomach. Recurrence after removal is, for obvious reasons, seen only in cancer of the rectum.

Cancer of the Liver.—This is generally secondary, but primary growths do occur, though rarely. Primary cancer is seen in the form of large tumors, with the usual alveolar structure varying in hardness. The precise origin of these cancers is not always clear. But the record of cases of primary cancer of the liver published within the last few years, leads to the conclusion that there are two distinct forms of this growth. The commoner form is much like a simple adenoma, having a tubular gland structure with columnar epithelium, though it may be highly malignant. This form has been thought to originate in the epithelium of the bile-ducts. The second and rarer form shows cells resembling liver-cells irregularly arranged, or with an imperfect acinous structure. This would seem to originate from the liver-cells proper, and thus to correspond to the primary cancer of other glands.

Secondary cancer is derived most frequently from a primary growth in the gastro-intestinal tract; but cancer of any part of the body may produce secondary tumors in this organ.

Every kind of cancer may thus be represented in the liver, but that most frequently met with is a soft, rapidly-growing cancer with alveolar structure, having the appearance called medullary. It causes immense enlargement of the organ, the largest livers met with (twelve or fifteen pounds, or even more) being produced.

The tumors are nearly always seen on the surface of the organ, where they form raised masses with a depressed or "umbilicated" centre.

Varying degrees of hardness may be met with till we come to a cancer so hard as to be called scirrhus. Nevertheless a tumor presenting the stony hardness and cicatricial atrophy of mammary scirrhus, is, if it ever occurs, extremely rare.

When the primary cancer is situated in the region of the portal venous system, the germs are probably always conveyed through this system, and distinct cancerous embolism of portal vessels is sometimes seen. In other cases the path of infection is not so clear, but it is probably through the arterial system. Cancer of the kidney has been known to reach the liver by first causing cancerous thrombosis of an adjacent mesenteric vein, and thus entering the portal trunk.

The secondary cancer sometimes occurs in minute growths so generally disseminated through the organ as to form a "cancerous infiltration."

The question has been raised whether the liver-cells take part in the formation of secondary cancer. Some hold that they are converted by infection into cancer-cells; some regard the latter as entirely formed by proliferation of cells derived from the primary growth. This is a disputed point, not ripe for positive decision; but the writer decidedly inclines to the latter view, believing that the liver cells merely undergo hypertrophy, while the bloodvessels and connective-tissue are used up in forming the stroma of the new-growth.

Cancer of the Lung.—Primary cancer is so rare that it must be doubtful whether it ever occurs; that is, in those cases where the lung has been apparently the only organ affected, there may have been some primary cancer elsewhere overlooked. Ziegler, however, refers to some cases.

Secondary cancer occurs in two forms—(1) as an infiltration spreading from the bronchial or mediastinal glands. But the histology of these forms is doubtful, and according to our definitions, a growth rarely starting in lymphatic glands could hardly be called cancer, unless there were some embryonic misplacement of tissue.

2. By infection from some distant primary cancer. Cancer of the breast may affect the lung through the pleura, but in other cases the germs will be brought by the circulation, forming a cancerous embolism. Almost every form of cancer is represented in these secondary growths.

Cancer of the Kidney.—Primary cancer of the kidney forms large masses which preserve in a remarkable degree the natural outline of the organ, and are generally strictly limited by the capsule. Very large tumors may be, however, thus formed. The consistence is nearly always soft and medullary. The cells are notable for their generally small size. In several cases where the origin of these growths was minutely examined, they were found to begin with hyperplasia of the renal epithelium, and tube-formation, so that the new-growth resembled an adenoma. This is, therefore, probably the way in which all originate.

Very large congenital tumors of the kidney sometimes occur in infants, and may even reach so large a size during fœtal life as to obstruct birth. They have been generally described as cancer, but perhaps would now be called sarcoma.

Cancer of various forms may occur in the kidney secondarily to growths in other organs.

In these cases the cells appear to be carried by the circulation into the Malpighian tufts, and there to form a species of embolus, from which the secondary growth originates, as in the case of the adenoma figured on p. 200.

Cancer of the Uterus.—Growths thus called are of two chief kinds:

1. Flat-celled epithelioma, already spoken of.

2. True carcinoma, which alone we describe here. The naked-eye appearance of the two is very similar.

The true cancer of the uterus usually begins in the cervix, more rarely in the fundus. It is very liable to necrosis and ulceration. Its consistency is usually soft, but varying in hardness. The alveolar structure of mature cancer is generally to be recognized; but if the origin of the growth be minutely examined, it is traceable to an overgrowth of glandular epithelium. Hence it is a form of adeno-carcinoma.

Metastasis to other organs occurs much more frequently than in the squamous-celled cancer of the os uteri.

Cancer of the Ovary.—This has, in early stages, a marked adenomatous character, resembling the cystic adenoma; but in some cases a great variety of epithelial cells is met with. It may be the starting-point of secondary tumors.

Cancer of other Glands.—The pancreas, the salivary glands, the testicle, may all be the starting-point of malignant growths, which, when fully developed, have the alveolar structure characteristic of cancer and epithelial cells. When minutely studied, their origin can generally be traced to hyperplasia of the epithelium of the glandular tubes or acini.

Cancer of the Thyroid, and other blood-glands with closed follicles, is also known, which has, in all probability, an analogous mode of origin.

Cancer of Bone and Connective-tissue.—The question, whether true cancer with epithelial cells can originate in bone, is a difficult one. Nevertheless growths are, in very rare cases, met with in bone having a structure indistinguishable from those arising from glandular epithelium. Such have been seen, for instance, in the os ilii. The explanation probably is that a portion of embryonic tissue from some glandular organ was displaced from its connections and included in the bone, just as rudiments of bone or cartilage become included in the testicle or parotid (*see* page 213).

In any case, these instances are too rare and exceptional to modify the general principle of classification of new growths stated above.

Certain special forms of cancer must also be noted.

Scirrhus or Hard Cancer.—This name is given to cancers in which the stroma is greatly developed, and consists of very thick and hard bundles of fibrous tissue, while the cells suffer atrophy.

Cancers are sometimes classified with reference to this character, as scirrhous and medullary, or hard and soft, medullary meaning those in which the cells predominate and the stroma is scanty. But, since this is a question of degree, it is not a good basis for classification. Many of what were once called medullary cancers are now called sarcoma.

Scirrhus occurs chiefly in certain situations, as the breast, the rectum, the pylorus. Scirrhous cancer of the breast is notable for its malignity.

Colloid Cancer (formerly called Alveolar Cancer).—In this the tumor undergoes colloid degeneration (*see* page 158), which chiefly affects the cells, and thus the alveoli may contain only homogeneous colloid substance with vestiges of cells. But it may affect the stroma also. These cancers are translucent and gelatinous, resembling myxoma in outward characters, though the anatomical distinction between the two is obvious. The form in which the stroma is chiefly affected by the colloid change, the cells being altered only in a subordinate degree, has been called carcinoma myxo-matodes.

Colloid cancer is almost confined to the abdominal organs, affecting the intestines and peritoneum chiefly. It may also occur in the mamma primarily, and in other parts as a secondary growth, or, in excessively rare cases, primarily.

Two views have been taken with regard to colloid cancer, either that it is a degeneration of ordinary cancer, or that it is a form distinct from the beginning. The former view is supported by the occasional occurrence of forms in which the colloid is combined with simple cancer of the medullary variety, but the latter view is probably correct. The reason for thinking so is, that, in many cases, the very earliest colloid growths which can be traced present this characteristic metabolism, and that the same property belongs to secondary growths derived from them. This mucous metabolism would then be an original endowment of the cells forming the cancer. These cancers are so rare that it is difficult to ascertain with precision where they originate. But, bearing in mind what was said before about the reproduction in cancers of the physiological properties of the tissue in which they arise, it may be plausibly conjectured that the peculiar properties of colloid are due to their starting originally from muciparous glands. Considering, however, that they sometimes appear to arise in the peritoneum, this view is only hypothetical.

Colloid cancer is not generally considered to be extremely malignant. Nevertheless, there are many instances of its being in a high degree locally infective, and giving rise to numerous secondary growths in distant parts.

CHAPTER XXIII.

CYSTS AND TERATOID TUMORS.

THERE remains for consideration a certain class of new productions which, not strictly tumors, nor, generally speaking, new-growths, are usually considered along with the latter, namely, those structures called cysts.

Under this head are comprised objects so different in origin and nature that it is somewhat illogical to call them all by the same name: and, indeed, the inclusion of them in one class is rather a matter of convenience than of scientific order. The only character common to all cysts is to consist of a cavity with a distinct wall containing fluid or semi-fluid material, so as to assume a more or less spheroidal shape.

The name is not given to normal parts of the body having this structure, such as the closed follicles of the thyroid or similar glands, unless they are enlarged or in some way altered from their original structure; and it is not customary to call a temporary cavity, such as an abscess, though it may correspond to the above definition, a cyst; but there is a little inconsistency in the application of the term, and its limitations are, to some extent, a matter of convention. A new-growth which produces or contains cysts is called *cystoma* or cystic tumor; but this name should not be applied to a single cyst.

Component parts of Cysts.—Every cyst, as thus defined, consists of two parts, the *wall* and the *contents*. The wall is composed chiefly of connective-tissue, either distinctly separable from the surrounding tissues, or else a part of them. It is often lined with epithelium, but the presence or absence of this structure depends upon the mode of formation of the cyst, as will appear in describing the different kinds. Such a lining, if present, is never produced entirely *de novo*, but is a development of the epithelium of the part in which the cyst is formed. Thus a cyst produced by breaking down or softening in the midst of connective-tissue will have no epithelium; but a cyst formed, as many are, from a glandular organ, will have one derived from the glandular epithelium of the original part; the character of which—ciliated, columnar, or spheroidal—it usually preserves. It will often also show its characteristic metabolism—fatty, mucous, and so forth. But sometimes the characters are lost or altered, and secondary changes may be brought about either by the effects of internal pressure or of injuries.

The *contents* of cysts are very various, and depend upon the nature of the parts in which they take their rise. There may be serous fluid, mucus, blood, colloid or gelatinous material, or masses of fat. But all must either be, or have been at one time, fluid; since the spherical or spheroidal form of a cyst is physical evidence of the fluidity of the matter contained in it. It happens, however, not unfrequently that by absorption or concentration the contents become semi-solid or gelatinous. The specific secretions of the parts in which cysts arise, such as sebaceous matter, milk, or bile, are often among their contents. Masses of cells, derived from the lining epithelium and other morphological products, may also be present.

Since all the peculiarities of cysts are referable ultimately to their origin and mode of formation, these differences form the only convenient basis of classification.

Classification of Cysts.—The chief forms of cysts may be enumerated as follows:

I. Cysts produced in a pre-existing cavity, hollow organ, or part lined with epithelium by accumulation and retention of its natural secretions. This may take place either (*a*) by closure of the natural opening, such as the duct of a gland or orifice of a tube, or (*b*) in cavities naturally closed, such as the follicles of the thyroid or ovary. They may be called *cysts of retention.*

II. Cysts formed out of embryonic rudiments of tubular or glandular structures imperfectly developed or closed during fœtal life—*developmental cysts.*

III. Cysts produced by softening in solid structures, or *cysts of disintegration.* These may have a distinct wall, but will not be lined with epithelium.

IV. Cysts produced by dilatation of connective-tissue spaces or lymphatics in connective-tissue. They will be lined with endothelium, and may be called *endothelial cysts.*

V. Cysts resulting from a continuous process of formation in a mass of solid tissue, so that they appear to arise in the wall of those already existing. These are called proliferous cysts or *cystoid tumors.*

VI. Cysts formed by inversion of the integument of the body at an early period of development, known as *dermoid cysts.*

In addition to these we have what are called parasitic cysts; *i. e.*, those formed round cystic parasites imbedded in the tissues. In these cases there is a sort of capsular or fibrous investment, which, being a part of the body, may be called a cyst; but since the cystic form is produced by the parasite itself, it is better not to reckon these structures among cysts properly so-called.

Class I. **Cysts of Retention.**—Cysts formed by accumulation or retention of secretions naturally most often occur in glands when the duct is from any cause stopped up. So long as the gland goes on secreting, there is naturally an accumulation of fluid, which dilates first the duct and afterward the gland follicles. This will go on increasing till the pressure, or an alteration in the gland follicles, puts a stop to secretion.

The most familiar instance of this process is seen in the sebaceous or atheromatous cysts of the skin. These arise from blocking of the orifices of sebaceous glands, either free or those connected with hair-follicles. As the gland goes on secreting, the sebaceous matter and glandular epithelium accumulate. Hence such cysts come to contain a thick gruel-like fluid (atheroma), consisting of fatty granules, plates of cholesterin, and a variable amount of glandular epithelium and epidermic scales. The original orifice may become so completely obliterated that the cyst appears an absolutely closed cavity. It may also be sometimes situated rather in the subcutaneous tissue than the skin, and connection with a sebaceous gland may appear doubtful. Possibly, in such cases, the cyst originated in an embryonic interpapillary process of epidermis which was the rudiment of a hair-follicle, not from the perfect follicle or sweat-gland. The structure will then approach very nearly to that formed by an introversion of a portion of the whole skin, or a *dermoid* cyst, which will be described farther on. Rudimentary hairs are sometimes found in sebaceous cysts.

The simple or compound glands on mucous surfaces often give rise to cysts by retention of their secretions. The commonest cause of obstruction of the orifice of the duct in such cases is chronic catarrhal inflammation of the mucous surface.

They occur, for instance, on the lips, on the inner surface of the mouth, and on the tongue, especially at the posterior part, where there are large glands.

Another class of similar productions is found on the mucous membrane of the stomach and intestines, sometimes small and very numerous, more rarely larger and scattered.

Larger and more distinct cysts arise from obstruction of the ducts of the salivary gland, forming what is called *ranula*. A similar condition has been observed by Virchow in the pancreas. Recklinghausen has shown that it is the duct of the gland in these cases which first undergoes dilatation while the gland goes on secreting.

Obstruction of bile-ducts in the liver gives rise to cysts containing bile, which is usually inspissated and mixed with much cholesterin. When the gall-bladder itself becomes distended by obliteration of its duct, it is sometimes spoken of as a cyst.

The name is given, perhaps with more propriety, to a dilatation from obstruction of the vermiform appendix of the cæcum.

Several forms of cysts are found on the mucous surface of the female genital organs. Those occurring on the *portio vaginalis*, or cervix of the uterus, form bladder-like structures with watery contents, which have received the name of *ovula Nabothi*, and similar structures may occur on the inner surface of the uterus itself, or less commonly on the vagina. Cysts may also arise by dilatation of Bartholini's glands.

Cysts may also be produced on the mucous membrane of the respiratory tract, most commonly in the larynx, by dilatation of mucous glands. Cysts in the kidneys are often formed in chronic interstitial inflammation of those organs, through obstruction of the uriniferous tubules, caused apparently by contraction of the newly formed fibrous tissue. These cysts are often minute and extremely numerous, but the precise process by which they are formed is somewhat obscure, and involves questions which cannot be considered here. Another kind of cystic formation in the kidney, apparently congenital, will be spoken of presently.

Cysts formed by retention of products in closed follicles are seen only in the thyroid and the ovary. In the first-named organ, though it is not generally called a secreting gland, mucous or colloid substance is produced in the follicles by metabolism of the epithelium, and removed apparently by the lymphatics. When this substance accumulates (whether by excessive production or by imperfect removal cannot be said), cystic dilatation of the follicles takes place. If the walls of the neighboring follicles become absorbed, as sometimes happens, cystic cavities of an inch, or even some inches, in diameter may be formed, containing liquid or gelatinous substance or fat. This constitutes the cystic form of goitre or bronchocele.

Cystic formation in the follicles of the ovary is to a certain extent a physiological process. That is to say, the swelling and ripening of each follicle during ovulation produce a kind of cyst, which under normal circumstances bursts. When, from some cause not clearly understood, the cavity remains entire and exudation continues, a cyst is formed, called a *simple* ovarian cyst, to distinguish it from compound ovarian tumors. These cysts are usually small, but in rare cases have been seen as large as a child's head or larger.

Class II. **Cysts formed out of Embryonic Rudiments** or **Developmental Cysts.**—Certain organs of the body are at an early period of development composed of tubes, which afterward become converted into closed cavities. The thyroid is an example. Now, if a portion of the embryonic tubular stage of an organ continue into later life, cysts may in like manner result from a transformation of these rudimentary tubes. This is probably the explanation of certain cysts, which are often found on the broad ligaments of the uterus and in the neighborhood of the ovaries and Fallopian tubes. Some of these appear to arise in the parovarium, a rudimentary tubular structure in the broad ligament, which remains as a relic of the "Wolffian body" or *mesonephros*, an embryonic organ which, in mammalia, precedes the permanent kidney and generative apparatus. Small cysts derived from the parovarium are very common, and some of considerable size are occasionally met with. The terminal portion of Müller's duct is dilated into a cyst, the so-called hydatid of Morgagni, and the same name is given to a corresponding structure in the testicle. It would not be possible here to enter into the anatomical details necessary to explain how these cysts arise. Their occurrence is mentioned because they throw light on a general process of cyst-formation which is important in other cases also. This process consists in the separation or pinching off of a portion of embryonic tubular organs, which portions then become dilated into cysts. The process differs from that of cyst-formation by simple retention of secretions, because it begins during embryonic life, and the structures thus formed are accordingly congenital. A remarkable instance of this kind is seen in the congenital cystic kidney. The organ at birth is found to be in a state of so-called "cystic degeneration," being converted into or made up of a mass of cysts, in which the proper secreting structure is lost. Such kidneys may reach a very large size, so as even to be an impediment to birth.

A similar condition is, rarely, met with in the adult kidney, of which the explanation is probably the same—that is to say, it is congenital in origin, and due, as is the other form, to cystic degeneration of rudimentary tubes, not of those completely formed. Virchow, however, refers the congenital cystic kidney to obstruction of uriniferous tubes by inflammation during fœtal life.

A similar condition sometimes met with in the testicle may admit of a like explanation, and perhaps, though more doubtfully, the very rare cystic degeneration of the liver which has been found to accompany the cystic kidney.

A certain class of cysts in the testicle, called spermatocele, containing spermatozoa, appear to arise from distention of detached portions of seminiferous tubes, which through some error of development have failed to become connected with the excretory ducts.

A certain class of cysts found in the ovary show their origin from a fœtal condition very clearly, by being lined with ciliated epithelium. The perfect ovarian follicles contain no epithelium of this kind, but the tubes of the Wolffian body, which was the embryonic basis of the ovary, as of other parts of the genito-urinary tract, were ciliated. Hence, these cysts are with much probability regarded as being formed from remnants of the Woffian body preserved in the mature ovary, not from the ovary itself.

The serous cysts of the neck, called hygroma colli, are referred to a metamorphosis and dilatation of a portion of the congenital fistula sometimes met with in those parts, which forms a more or less perfect communication between the surface of the neck and the pharynx; representing, in fact, a persistent portion of one or other of the original branchial clefts.

Class III. **Cysts of Disintegration.**—Cysts produced by softening in the midst of a solid organ are very various in origin, and so different in appearance that they can hardly be included under one head. As an example, let us suppose that a portion of brain softens and dies from its blood-supply being cut off or other injury. The necrosed tissue is never restored, but being gradually absorbed and the surrounding parts being unable to collapse completely, a cavity is left, which is filled with serous fluid, shut in by a sort of fibrous capsule. Such a cavity it is customary to call a cyst produced by softening. When blood is extravasated in the brain, it may be quite or nearly absorbed, and a similar cavity may ultimately result, which is called a hemorrhagic or apoplectic cyst. It is evident that in most organs the physical conditions are not such that a cavity of this kind would be produced by the same process, as the destroyed part would collapse and form a scar. The term cyst is not therefore very appropriate in these cases. Softening of the bone, in the disease called osteomalacia, may give rise to similar structures.

In many new-growths, especially in sarcoma and chondroma, the softening of certain portions often produces cysts, and hence we have the mixed forms of tumors called cysto-sarcoma, cystic chondroma, and so on. But in tumors of glandular organs, cysts may result from a process of formation more resembling that of the cysts formerly described, by obstruction and dilatation of glandular acini.

Class IV. **Endothelial Cysts.**—In fibrous structures cavities containing serous fluid are often produced by chronic irritation, and probably owe their origin to dilatation of the original lymphatic spaces of the fibrous connective-tissue. The bursæ formed in the neighborhood of joints or other bones may be regarded, when they are of new formation, as cysts of this kind. Ganglion, in the sheaths of tendon, is a less perfect example of the same kind.

Cysts containing Air.—In this class must be placed the exceedingly rare cystic structures produced by the enclosure of bubbles of air in fibrous tissue. Multiple cysts of this kind containing air were described by Jenner and Hunter as occurring on the intestines of pigs, and specimens are preserved in the Hunterian Museum. Almost the only example from human pathology is one described by the writer some years ago. A number of pedunculated cysts, arranged in clusters like bunches of grapes and containing gas, were found attached to the peritoneal surface of the intestines. The contents were found to be essentially atmospheric air partially deprived of oxygen, which had apparently made its way during life along the intestinal walls beneath the serous coat from an ulcer of the stomach. The serous coat was then at certain points pushed out in the form of cysts, which were not mere temporary expansions, but definite and permanent fibrous structures, which might be compared to serous cysts in connective-tissue.[1]

Class V. **Cystoid Tumor, or Cystoma.**—The only class of cysts which are, strictly speaking, to be regarded as new-growths, are tumors in which there is a continual production of new cysts; hence called *proliferous*. These structures are almost exclusively found in the ovaries, where they constitute the well-known and formidable ovarian tumors.

It has already been mentioned that cysts, rarely of a considerable size, may be formed by dilatation of the Graafian follicles of the ovary. These may be numerous, so that the condition may be described as cystic degeneration of the ovary; though each cyst for itself is a simple structure.

But in the proliferous ovarian cysts, which we have now to speak of, there is actual new growth. This new growth may be of two kinds. In the rarer and simpler kind a papillary growth takes place into the interior of the cyst, which may project upon its inner surface as a papilloma of the skin does upon the surface of the body. Sometimes the papillary growths may grow through the wall of the cyst and project into the peritoneum. It is remarkable that the inner wall of these cysts is sometimes lined wholly or partially with ciliated epithelium. This fact, together with other considerations, has led some pathologists to think that these cysts do not arise from the Graafian follicles, but from portions of the parovarium, or other remnants of the Wolffian body, enclosed within the ovary. This, though not universally accepted, seems the most probable explanation. This form of tumor is called *cystoma papilliferum*, or papillary cyst of the ovary (Doran).

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[1] Trans. Pathological Society, vol. xxii. p. 330. The specimen is in the museum of St. Mary's Hospital.

The commoner kind of compound proliferous ovarian cystic tumor forms a mass of variable, but sometimes of enormous size, which on section is found to consist of an immense number of larger or smaller cysts, containing fluid which in the smaller is generally thick, tenacious, and of gelatinous appearance, while in the larger it is thinner and more resembles serous fluid. It is often stained red, or of various colors, as the result of hemorrhage. The walls are of variable thickness, but there is an intermediate tissue of solid consistency, the structure of which throws much light on the origin of the cysts. In this tissue are contained a large number of small cavities, lined with cylindrical, non-ciliated epithelium which precisely resemble the acini of glands, so that if the solid portion of the tumor were alone regarded, it would be described as an adenoma or glandular tumor. On examining the mode of growth of these tumors, it appears that they begin with the formation of glandular acini, and that by secretion and accumulation of fluid within these glandular structures the cysts are formed. Now if we suppose one such cyst to be produced, and reach a considerable size, it will be evident that its walls will consist of, or at least contain, the glandular tissue. Hence. when new cysts are formed out of this tissue they will appear to be, or in one sense will be, produced by the wall of the cyst already existing. It is for this reason that compound ovarian cysts are spoken of as proliferating, or as having the power of producing new cysts in their walls. Some of the larger cavities appear to be formed by rupture of the walls of adjacent cysts: and it is possible there may be an extension of the cavity into the neighboring tissue by tubular or acinous prolongations. The cylindrical epithelium is naturally less clearly marked in large cysts. Without entering into minute details, it may be taken as established that even the largest compound ovarian cysts of this class have their origin in glandular tumor-tissue.

Now as no glandular tissue is contained in the mature healthy ovary, the question arises, Whence does this tissue itself originate? The origin clearly must be from an early or embryonic condition of the organ. In the development of the ovary the Graafian follicles are formed by certain cells arranged in the form of tubes (Pflüger's tubes), which sink into the stroma of the organ, and there become separated or cut off, so as to form closed follicles. At a certain stage, therefore, the ovary may be compared to a glandular organ; and the compound cystic tumors may therefore be referred to as an abortive or imperfect development of the rudimentary follicles; unless there be, what is less likely, a recurrence of the embryonic formation in later life. They illustrate, therefore, Cohnheim's law that new-growths originate in residues of embryonic or imperfectly developed tissue in the different organs.

The name given to them is *cystoma glandulare* or *adeno-cystoma proliferum*; multilocular proliferous glandular cystic tumor.

These tumors may, as is well known, reach an enormous size, weighing fifty to one hundred pounds, or even more, and are often a cause of death. But they are not malignant, and have not produced secondary growths, except in one or two instances, when the secondary tumors were adenomatous. In a few rare instances, a tumor of this kind has been known to pass into carcinoma, as has been shown to happen in the case of adenomata derived from other glandular organs. It should be remembered that there is also an ordinary carcinoma of the ovary.

Dermoid Cysts.—Another class of cysts found in the ovary, but also in other parts of the body, is distinguished by having a wall composed of structure precisely resembling that of the external skin, though they may have no direct connection with it. They have been found, besides the ovary, in the peritoneum and in subcutaneous cellular tissue of several parts of the body, especially in the neck. Rarer situations are the orbit, the lungs, stomach, testicle, cranium, etc. In the more superficial situations the growth may easily be explained by an intrusion of a portion of epidermis at an early period of development, and subsequent separation of the intruded portion from the superficial layer.

This explanation will apply even when solid tissues, such as muscle or bone, lie between the cyst and the surface; since those tissues are of later formation than epidermis, and may therefore have grown in the position they occupy, after the cyst was formed. This view is confirmed by the fact that dermoid cysts of the face and neck are observed to occur either along the lines corresponding to branchial clefts, or in the middle line of the body—that is, in those situations where the integument remains longest open, so that during the process of closure a portion of skin might most easily be pinched in. The explanation of those more deeply situated is probably also that some germs of the epiblast or upper germinal layer have been misplaced at an early period of development; but the question is a complex one, and can only be alluded to here. There is no reason to think that dermoid cysts of the ovary originate in the Graafian follicles.

The *wall* of a dermoid cyst consists of a complete skin, with epidermis, which is, of course, placed internally, and a distinct corium, fibrous in structure, placed externally. Sometimes outside this is found adipose tissue, corresponding to the natural subcutaneous tissue. The skin is provided with its usual appendages, hair and sebaceous glands. Sweat-glands are less constantly found. The papillæ of the skin are not usually well developed.

The *contents* of the cysts consist of the accumulated secretions of the sebaceous glands, with more or less desquamated epidermis, and often a large number of hairs which are pale or reddish in color. Teeth, sometimes in very large number, are also occasionally found implanted in the wall, or free in the cavity. The sebaceous secretion consists of fatty matter in various forms. It is sometimes liquid at the temperature of the body, so as to be oily in consistence, and hence such specimens are described as "oil-cysts." In other cases the contents are a fatty emulsion of gruel-like appearance, often containing plates of cholesterin or fatty crystal (stearin and palmitin).

Rarer constituents are brain or nerve-tissue, striated muscle, cartilage, and bone. In these cases—chiefly ovarian tumors—there is a transition to the form of tumor next to be described.

Dermoid cysts are probably always congenital, but go on increasing in size, usually slowly, but sometimes, at the epoch of puberty, rapidly. The largest specimens, even up to 20 pounds in weight, have been found in the ovary. Those from other parts of the body are usually small, but Dr. Ord has described one weighing 14 pounds from the abdomen of a man.

Teratoid Tumors, or Teratomata.[1]—This name is given to certain new-growths of very complex structure, consisting not of one or two kinds of tissue only, like those which have been already spoken of, but containing a confused mass of connective-tissue, cartilage, bone, muscular and nervous tissue, as well as epithelial products, such as skin, hairs, and glandular tissue. Together with these is usually, if not always, some embryonic tissue of undeveloped character, resembling a sarcoma. These tumors have a great scientific, though not much practical, interest, and are, as compared with simple tumors, very rare. They are always of congenital formation.

Such tumors may be broadly divided into two classes: (1) those which are formed by a combination of structures derived from different embryonic layers of one individual; (2) those which are formed by the inclusion in a perfect individual of portions of an imperfectly developed twin embryo.

1. Masses composed of several different kinds of tissue may be produced by transposition, during embryonic life, of masses derived from different layers of the blastoderm. We have seen how such a transposition may give rise to heterologous growths, such as that of bony or cartilaginous tumors in the testicle, or muscular tumors in the kidney, or dermoid cysts in internal parts. By a further complication of the same process, it is easy to see that more complex tumors might arise. A confirmation of this hypothesis is that these complex growths are most often found in those parts where abnormalities and misplacements of embryonic tissue are especially apt to occur; namely, in the genito-urinary tract, and especially in the ovaries, sometimes also in the testicle or in the peritoneum, very rarely elsewhere. In the ovary, masses of mixed structure may be combined with a dermoid cyst, and such cysts are strictly to be regarded as teratoid tumors. Waldeyer has suggested that such ovarian tumors are produced by an aberrant activity of the reproductive function of

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[1] The word teratoid is derived from the Greek τέρας = a monster, since these tumors make an approach to monstrous developments.

the Graafian follicles; being, in fact, a sort of parthenogenesis, or asexual generation.

2. In the second class of teratoid tumors the mixed tissues are arranged in the form of imperfect organs; for instance, the rudiments of the vertebral column, of other parts of the skeleton, of intestine or of brain, may be found, and the variety of tissues will be absolutely greater than in the first class. Now it is clear that such a mass makes something like a transition to an imperfectly formed fœtus or second individual, and hence may very reasonably be regarded as the remains of an abortive fœtus, which, had it been somewhat more developed, would have been a so-called "parasite," or not separated twin, or "monster by excess." This theory is further confirmed by a consideration of the situation in which these tumors are found. By far the greater number occur in connection with the sacrum, where they either project externally or are included within the body-cavity; and with regard to tumors in this situation, at all events there is a strong probability in the theory that they represent an abortive parasitic twin-fœtus. Many of these "congenital sacral tumors" have been observed, and their structure is, in most cases, somewhat like what has been described. Other situations for these tumors are the mediastinum, the skull, the peritoneum, the ovary, and even the testicle. But it is impossible to say whether, in all these cases, the new-growth is the product of the twin-embryo. However, from the sacral tumors transitional forms might be traced to parasitic imperfect fœtuses, and even up to the well-known cases of twin individuals whose bodies are inseparably attached. But this comparison would lead us into the subject of malformations and monsters, which it has been decided not to include in the scope of this work.

CHAPTER XXIV.

GRANULATION-TUMORS OR INFECTIVE GRANULOMATA.

There is a class of new formations which has been sometimes regarded as belonging to new-growths properly so-called, sometimes as inflammatory products, and sometimes as intermediate between these two groups. There can be little doubt that they are most nearly related to the products of simple inflammation.

These formations are distinguished from others, and agree among themselves, in (1) their structure, (2) their mode of growth and clinical characters.

1. **Structure.**—These formations are chiefly made up of lymphoid corpuscles or leucocytes, which, taken individually, are indistinguishable from the corpuscles of inflamed parts. Besides these, there are larger cells, like those of granulations, called formative or *epithelioid* (a name to be used with caution, as it may mislead), and in some cases very large or "giant cells"—viz., masses of protoplasm containing several nuclei.

The whole structure is somewhat like that of granulations, or at least does not go beyond that degree of development. It forms no perfect tissue except fibrous scar-tissue. There is in some cases a lymphatic reticulum or stroma.

These formations differ from the products of common inflammation in their relative *permanence*, which is intermediate between the transitory nature of ordinary inflammatory products and the persistence of true new-growths. They are also notable for the tendency to form limited foci or masses, in contradistinction to diffuse changes. Both the connective-tissue and epithelial elements of the tissue in which they occur, but especially the former, show some signs of overgrowth; still a great part of the new formation is composed of extravasated leucocytes.

2. **Mode of Growth.**—These formations begin to grow in most cases at one part of the body; and for a longer or shorter time remain local, but may afterward become widely distributed and pass into a general disease.

Several of them are capable of being transmitted by inoculation. In most of them a parasitic microörganism has been found, which is either itself the irritant or produces some substance which acts as such. Each focus of disease is infective—that is, has the power of setting up other like foci of disease in its neighborhood.

They have thus a marked affinity to the general infective diseases. Some at least of them are already found to be the products or the "anatomical expression" of such a disease. They differ from the acute specific fevers in two respects—(1) in having a very long period of evolution, which may be, in fact, not self-limited at all, but brought to an end only by the death of the individual. The difference must depend upon a difference in the vitality of the parasite producing the disease. In the acute infective diseases the parasite only lives for a certain time whether the patient dies or recovers. In these processes the parasite is able to live for indefinite periods in the organism. (2) Again the irritant or infective agent in the specific infective diseases when inoculated, at once enters the blood; while, in the processes here spoken of, it is, in the first instance, limited to certain spots, though it sometimes becomes more generally distributed afterward.

Definition.—We may then define these formations as chronic or persistent inflammations, produced at particular spots by the action of a continuously acting irritant, and spreading by the infection of neighboring parts and by the circulation. The special peculiarities of each, as compared with inflammation and with each other, depend upon differences in the nature of the irritant. This irritant is in most cases certainly, in all probably, a parasitic microörganism, or something produced by it.

Objections.—A difficulty at once arises in this view of the subject, which has been brought before me by students. Why are the phenomena in these cases so different from the phenomena of what we call common inflammation as formerly defined?

The answer to this is—that in the latter we are speaking of the action of mechanical, physical, or chemical irritants. The former are very large in proportion to the cells. Even the smallest mechanical lesion destroys many cells or other elements, the appearances called inflammation being produced in those which escape destruction.

The micro-parasites are smaller than cells, and if regarded as mechanical irritants, may act on cells without destroying them. A structure much like a tubercle is produced by implanting a very small foreign body, *e. g.*, a hair, in the rabbit's eye, but differs from true tubercle in not having any power of infection, so as to produce other similar bodies. Again the physical and chemical irritants, even when applied in the most delicate manner possible, act over areas which are, relatively to the cells, very large. They cause destruction of tissue-elements, and, as in the case of mechanical lesions, the effects called inflammation are produced just outside the area of destruction. But the chemical substances produced by the microörganisms are present in minute quantity and act at insensible distances. Hence they affect the tissue-elements directly, without at once destroying their vitality. We may sum up these differences by saying that the irritant in these processes is *molecular*, while in the grosser forms of inflammation it is *molar* or *massive*.

Again, we must remember that the irritation is in these cases persistent—not like that of a wound transitory, of which the after-effects only or chiefly are perceived.

Finally, the irritation is not purely chemical or mechanical, but *special* (as is shown by inoculation of the specific virus), and differences are seen in the case of each different disease.

Another objection is that some of the elements of the granulation-tumors are different from the cells found in common inflammation: viz., the so-called epithelioid or formative cells, and the giant cells.

But the former have been shown to be generally present in the granulations of wounds, while the latter have also been found there as well as in other chronic inflammations; and have been even caused to grow experimentally by Ziegler.

If, instead of inflammation, we were to say irritative hyperplasia, the meaning would be virtually the same; the disease is, at all events, the result of some living persistent virus; and until such a virus is demonstrated in each case, the history of the growth is incomplete.

The formations included in this class are tubercle, the products of syphilis, of leprosy, and of glanders, lupus, rhino-scleroma. It is probable that this list will be enlarged.

In the present state of science, it is a little difficult to say where the infective granulation-tumors should be placed in a systematic work. They may be treated of as forms of inflammation, or as a sub-class of new-growths, or, with reference to their cause, under the head of specific infective diseases. We have thought it best to place them under the latter head, as diseases produced by specific poisons, and their further consideration is accordingly deferred to the later part of this work.

CHAPTER XXV.

QUALITATIVE VARIATIONS IN THE BLOOD.

IN an earlier part of the book (Chapters II., III., and IV.) variations in the *quantity* of the blood and disturbances of the circulation were spoken of, but the *qualitative* composition of the blood and its variations are also important factors in general pathology. Therefore, although these changes are not, strictly speaking, included among the processes of disease, it is right that a short account of them should be given here. Variations in the amount of water contained in the blood will be first considered, then variations in the corpuscles, and lastly alterations in the other constituents.

Conditions of the Blood generally called Anæmia or Spanæmia.—If the proportion of water be increased in proportion to all other constituents, the condition is called *hydræmia*. If the serum of the blood contain an abnormal proportion of water, that is, be of low specific gravity, it shows a deficiency of serum-albumen ; this condition has been called *hypalbuminosis*. If the proportion of colored corpuscles be diminished, the condition is called *oligocythæmia* or *aglobulism*. A similar diminution in the leucocytes might, if it required a distinct name, be called *oligoleucocytosis*. It is possible that, whether the number of blood-disks are diminished or not, the proportion of hæmoglobin in the blood may be reduced. This condition is one of great importance, and has no convenient name, but might be called *achromatocythæmia*, or more shortly *achromatosis*.

These several conditions, which are included under the wide and lax term anæmia, or spanæmia, must be considered separately.

Hydræmia.—An excessive proportion of water in the blood may arise (1) from an increase in the total amount of water present in the circulatory system, the other constituents of the blood remaining unaltered, which, of course, involves an increase in the whole mass of blood ; or (2) from an increase in the proportion of water, the mass of blood remaining the same. In this case the other blood-constituents (albumen, corpuscles, etc.) must of course be diminished. In both cases the density of the blood is lowered.

1. The former condition may be called *hydræmic plethora*. It is evident that, as a transitory condition, it must often occur ; since the amount of water in the blood depends upon the balance between the water supplied, viz., in food and drink, and that excreted, viz., by the kidneys, lungs, bowels, and skin. If it be supplied more rapidly than it is excreted, it must accumulate in the blood. But both practical experience and experiment show that if the excreting organs be

healthy, the balance is quickly righted. Water, when ingested, acts as a sudorific and a diuretic, and stimulates the activity of all excretory organs. If the kidneys excrete an insufficient quantity of water (as is the case in some, but not all, kidney diseases) there must be an accumulation in the blood. There is no evidence that this is the case when the excretion from lungs or skin is hindered.

In experiments on dogs (animals which sweat very little) large quantities of saline solution have been injected into the vessels; and even as much as three times the normal volume of blood may be added without permanent results. Excretion rapidly takes place by the kidneys, bowels, salivary glands, etc., and the flow of lymph in the lymphatic system is greatly increased. The actual density of the blood is also found not to diminish at all in proportion to the amount of fluid added. The rapidity of the circulation is much increased, but the arterial pressure shows only a transitory rise.

When much larger quantities are injected (amounting to 60 or 70 per cent. of the body-weight), death results; and after death extensive œdema of the abdominal organs is found, and of secretory glands, but not of other parts.

Hydræmic plethora probably exists in the human subject in cases of kidney-disease where the amount of urine is diminished; but cannot, in practice, be distinguished from the form of hydræmia now to be spoken of.

2. The other form of hydræmia, in which the solid constituents of the blood are diminished, may be called pure or atrophic hydræmia. It is produced when the albumen and corpuscles of the blood are too rapidly removed or inadequately renewed; it is therefore the condition commonly met with in several forms of anæmia. Serum-albumen is the most important constituent wanting. It is sometimes called *hypalbuminosis*. This of itself does not cause any increased activity of the excretory organs. This condition may be imitated experimentally by substituting salt-solution, injected into the vessels, for a corresponding quantity of blood which is withdrawn, so as to leave the whole volume of blood unaltered. In this case there is no increased secretion or transudation of water observed. The arterial pressure falls, and there is no acceleration of the blood-current. This condition may be produced by anything which causes a loss of albumen, as hemorrhage, albuminuria, excessive lactation, etc. It is also said that diet deficient in albumen produces this, while inadequate general nutrition produces simply atrophy.

These two forms of hydræmia have therefore very different consequences, though it is not generally possible to distinguish them during life, since we have no means of measuring the quantity of blood in the body; and all we can measure is the density, which indicates the proportion of water.

Hydræmia.—The proportion of water in healthy blood may be estimated at 780–800 parts per 1000.

A slight increase of this proportion, viz., to 800–820 parts per 1000, occurs after temporary abstinence from food, in the early stages of acute diseases, and in most chronic diseases. An increase up to 820–880 per 1000 occurs in starvation, and in most wasting diseases, and in most of the states clinically recognized as anæmia. Thus in chlorosis a proportion as high as 868.7 has been observed, and an average of 853.2 (Andral and Gavarret). In another series of cases of chlorosis, an average proportion of 828.1 per 1000 was found (Becquerel and Rodier). In cases of advanced heart-disease the proportion though raised, was not so high, viz., 815.8. In leukæmia it varies from 820 to 881.

The same relations have been exhibited in a different way by determining the specific gravity of the serum of the blood. This varies normally from 1027 to 1032, the average being 1028 (Gamgee). In chlorosis the mean has been found to be substantially the same as this, but in heart-disease it has been found as low as 1025, and in leukæmia 1023. But the most marked changes have been found in Bright's disease of the kidneys, where a density of 1013 in the serum was found; the researches of Christison gave numbers from 1019 to 1020, and Bartels gives 1018 to 1015.

The results just given rather indicate that form of hydræmia which we have called hypalbuminosis. The facts are also given by stating the amount of solid residue left by evaporation of serum. Normal serum contains nine or ten per cent. of solid matters, of which about eight per cent. is serum-albumen. These solids are generally diminished in Bright's disease and most wasting diseases, as well as in anæmia, and in chlorosis have been found as low as 7.5 per cent. and in a case of leukæmia 6.7 per cent.; in advanced heart-disease a mean of 7.16 has been found, and in one case the solids even sank to 5.24. The discrepancies between the results of this method and those showing the amount of water in the blood, of course depend upon differences in the other constituents of the blood, viz., fibrin and corpuscles.

The density of the blood as a whole will, of course, also vary. That of defibrinated blood varies in health from 1045 to 1062, but a specific gravity of 1075 would not be necessarily inconsistent with health (Gamgee).

It has been found as low as 1035 in chlorosis, and 1041 in Bright's disease. But in other cases of chlorosis there was a mean of 1045.8. In one case of leucocythæmia, it was as low as 1036, but in others hardly diminished; and in heart-disease the minimum observed was 1041, the average being 1050 or 1052. It thus appears that the density of defibrinated blood as a whole is a less satisfactory indication of its composition than the other methods given.

CHAPTER XXVI.

VARIATIONS AND MORBID CONDITONS OF THE COLORED CORPUSCLES OF THE BLOOD.

Oligocythæmia.—The condition in which the colored corpuscles of the blood are diminished is that which is most generally understood by anæmia. This deficiency may be produced (*a*) temporarily by any considerable loss of blood, or (*b*) permanently by any cause which interferes with the formation of colored corpuscles in the body. The way in which the first cause acts has already been explained (see p. 26). With regard to the second cause, it is at present hardly known except by its effects, since physiology has not yet explained to us how the blood-disks are formed, or how their inevitable waste is supplied.

A diminution in the colored corpuscles is noted in most of the conditions clinically recognized as anæmia, especially in grave idiopathic anæmia and less constantly in chlorosis, in starvation, in Bright's disease, and advanced heart-disease, after prolonged diarrhœa and dysentery; in malarial cachexia, in scurvy, in leukæmia, in chronic metallic poisoning, and in most chronic diseases.

The most conspicuous symptom of this condition is paleness, especially of the mucous surfaces, *e.g.*, the conjunctiva, but this does not of itself necessarily show that the number of corpuscles is deficient. It shows a deficiency of coloring matter—hæmoglobin; and this may be due to a deficiency of corpuscles. Nevertheless, the proportion of hæmoglobin and that of corpuscles do not always correspond, since the amount of that substance in each corpuscle may, in diseased conditions, vary very much, though it is nearly constant in health. The size and shape of the colored corpuscles are also found to be altered in cases of anæmia. These relations were studied many years ago, when bleeding was in fashion, on large quantities of blood, by direct weighing and measuring; and important results were obtained, especially by French investigators, Andral, Gavarret, Becquerel, Rodier, and others. More recently the method of numeration has been used with instruments, devised at first by Vierordt and modified by Malassez, Hayem, and others.[1]

Variations in Number of Blood-corpuscles.—The proportion of colored corpuscles in the blood is expressed by reference to a standard volume of blood—viz. one cubic millimetre. The average number normally contained in this standard volume is, in robust men, for blood taken from the finger about five to six millions; but may, in persons less robust, be as low as four and a half, or even less, without being absolutely abnormal. In disease this number is often greatly diminished. In extreme cases of fatal idiopathic anæmia a number as small as 414,062, or less than one-tenth of the normal, has been observed; in another, 820,400; in a case of purpura hæmorrhagica, 1,000,000; in malarial anæmia, 1,182,750; in extreme cases of chlorotic anæmia, 2,500,000 or 2,250,000; but in moderate cases of chlorosis the number may be only a little below the normal average, or even normal, notwithstanding the symptoms of anæmia are strongly marked, as will be explained below.

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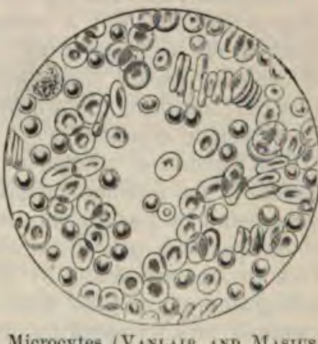
[1] The instrument generally used in this country is that called by Dr. Gowers the hæmacytometer. See, for a description of these instruments, Gamgee's Text-book of Physiological Chemistry, London, 1880, p. 74. Cornil and Ranvier's Pathological Histology, translated by E. Hart, vol. i. p. 48, 1882.

Variations in Size and Form of Blood-corpuscles.—In all anæmic conditions the size, and to some extent the form, of the blood-disks, are found to be altered. The normal average diameter of a human blood-corpuscle may be taken as about $\frac{1}{3000}$ of an inch, or 7.5 μ ($\mu = \frac{1}{1000}$ of a millimetre), but there are always found some having an average diameter of 8.5 μ, and some smaller, averaging 6.5 μ. In healthy blood there are about 75 per cent. normal, 12 per cent. larger, and 12 per cent. smaller. In anæmia resulting from a sudden loss of blood, these proportions are unchanged; but in all chronic anæmias the average size is diminished, and may be as little as 7 μ or 6 μ. This diminution is owing to the presence of a larger number of the ordinary small disks and of some which are very much smaller. These very small disks or *microcytes*, may have a diameter of 3 to 6 μ, or in rare cases as little as 2.2 μ. They have a remarkably deep color.

FIG. 66.



Microcytes (VANLAIR AND MASIUS, *Microcythémie*, 1871).

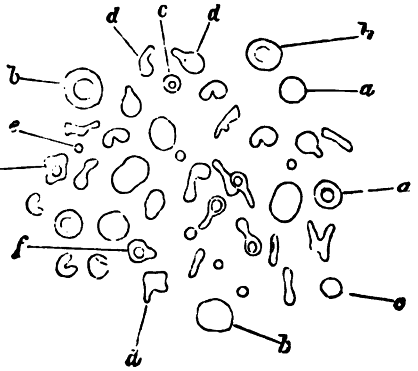
The small round brilliant spheres are microcytes. Normal blood-disks and one leucocyte introduced for comparison.

There are in anæmia nearly always found some larger than normal, having a diameter averaging 10 μ to 12 μ, sometimes even larger. The number of these *giant-disks* or *macrocytes* is, however, relatively so small that they do not raise the average diameter of the disks. It follows from the ordinary laws of solid geometry that the cubical contents or mass of each corpuscle is diminished in a still greater ratio than its diameter; and by a rough calculation 100 corpuscles of 7 μ in diameter will have a volume equal to 80 normal corpuscles only, and 100 of 6.5 μ in diameter are equivalent to 75 normal corpuscles in volume.

The shape of the small corpuscles, and sometimes of those of normal diameter, is often, in anæmia, somewhat oval instead of being circular, and many irregular forms are sometimes met with. This condition has been called Poikilocytosis (see Fig. 67)

Microcytes are more abundant in blood which has been taken out of the body for some time, or after death. Hence, they have been regarded as post-mortem productions, which is probably in part, but not wholly, true. I have certainly seen them in fresh blood. Even after death an abundance of them characterizes anæmic blood.

Fig. 67.



Various forms of blood-corpuscles in anæmia (Scheube)
a, normal; *b*, macrocytes; *c*, small disks; *d*, irregular forms; *e*, very small disks or microcytes; *f*, irregular nucleated corpuscles.

Variations in Coloring Power of Corpuscles.—The number of corpuscles alone is not a correct index of the degree or intensity of anæmia, clinically speaking. This arises from the fact that the amount of coloring matter (hæmoglobin) contained in each globule is also, generally speaking, diminished. This important fact is ascertained in the following manner:

The number of corpuscles in the standard unit of blood is ascertained, in the manner indicated above, by the hæmacytometer. Next the amount of hæmoglobin in the same unit is determined by a method of comparative color-determination, which cannot be described here.[1] This amount was found by Malassez to be from 0.125 to 0.134 of a milligramme in normal blood. In healthy blood the amount of hæmoglobin is, broadly speaking, in proportion to the number of corpuscles—that is to say, each corpuscle possesses the normal, or nearly the normal, coloring power. But in anæmic blood this proportion is altered—that is to say, each corpuscle may possess much less than its normal amount of hæmoglobin, and will appear under the microscope even visibly paler than natural.

If the maximum proportion of hæmoglobin in a healthy corpuscle be represented by unity, it is found that this proportion may be as low as 0.85 without any sensible departure from health. But in anæmic blood this may sink to proportions varying from $\frac{2}{3}$ to $\frac{1}{8}$ of the maximum.

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[1] See Gamgee's Physiological Chemistry, pp. 182–186.

In cases of moderate anæmia the proportion is usually from $\frac{1}{2}$ to $\frac{1}{4}$ of the maximum. This will evidently be partly due to the diminished size of the corpuscles, but this is not enough to explain the altered proportion.

The proportion of hæmoglobin may be conveniently expressed in terms of the number of healthy corpuscles which would be required to produce the same colorific effect. For instance, if the proportion of hæmoglobin, or the colorific intensity, be found to be $\frac{2}{5}$ of the normal, this will correspond to two millions of healthy corpuscles. If the number of corpuscles should be normal, each corpuscle must have only $\frac{2}{5}$ of its normal proportion of hæmoglobin or colorific power. But if the number of corpuscles should be found to be only four millions (say), then the colorific power, or proportion of hæmoglobin in each, would be one-half of the normal. Another way of stating the rule is as follows. The ratio of the percentage of hæmoglobin to the percentage of corpuscles gives the average value in hæmoglobin, or coloring power of each corpuscle. Thus, if the proportion of hæmoglobin be 40 per cent. of the normal, and the number of corpuscles in the standard volume four millions, that is 80 per cent. of the normal, then the fraction $\frac{40}{80} = \frac{1}{2}$ represents the average coloring power or value of each corpuscle.

The results obtained by these methods are very important. It is found that the number of corpuscles may be nearly or quite normal, even when the pallor and other symptoms of anæmia reach a high degree; but the colorific power of the corpuscles is much diminished. This is especially seen in some, but not all, cases of chlorosis. On the other hand, in some cases of extreme anæmia, when the number of corpuscles is exceedingly small, the colorific power of each corpuscle may be normal, or even greater than normal. Between these extremes various degrees of anæmia may occur, characterized by variations in the number, coloring power, and also in the size of the corpuscles. On this basis, Hayem has given examples of the degrees of anæmia in the following table:

DEGREES OF ANÆMIA.[1]

	Degrees of aglobulism.	Number of globules in cubic mm.	Coloring power of each globule.	Size of globules
0	Standard	5 to 6 millions.	1	Normal.
1	Slight	3 to 4 millions.	$\frac{1}{2}$	Normal.
2	Moderate	2 to 3 millions.	$\frac{3}{8}$	Many small.
3	Severe	800,000 to a million.	4	Many small.
4	Extreme	450,000 to 800,000.	1	Various.

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[1] In this table it will be observed that aglobulism (or aglobulia) is used for simple deficiency in the number of globules, independent of their quality. It should be noted that the relations here expressed between the degree of aglobulism and other results, such as coloring power and size of globules, are not general laws, but only the propor- tion found in particular cases.

Causes of Anæmia.—The several conditions above described may be produced by loss of blood, especially by repeated small losses.

Other causes are such as lead to wasting of the corpuscles or of the albuminous constituents of the plasma, and such as prevent the proper formation of new corpuscles or the renewal of the solid constituents.

Thus want of food and all wasting diseases tend to produce it, as also special agents, such as mercury, phosphorus, and other mineral poisons, and the poison of malaria. Privation of light has a marked influence in checking the formation of the colored corpuscles.

Certain forms of anæmia depend on special, though unknown causes.

Chlorosis is a special form, mostly found in young persons, and almost exclusively in the female sex, and often connected with defective evolution or derangements of the sexual system. It is, however, separated by no clear line from ordinary anæmia. Its most marked feature is achromatosis, with variable degrees of aglobulism, and the nutrition of the body is often good.

Idiopathic (or pernicious) anæmia clearly involves defective production of corpuscles, but the original cause of this fault is still to seek.

Malarial anæmia, though rarely seen in this country, often assumes the most extreme form.

The anæmia of kidney-disease is especially remarkable for showing hydræmia combined with hypalbuminosis, though the corpuscles also suffer.

Consequences and Symptoms of Anæmia.—Pure anæmia produces great muscular weakness and failure of the heart, leading to syncope. The nervous system is often over-excited, producing convulsions and delirium.

Hydræmia, especially when accompanied by hypalbuminosis, lowers the nutrition of the body generally, and has an undoubted tendency to favor effusion of serum in the tissues, or dropsy, as was explained above (p. 47).

When the colored corpuscles, or hæmoglobin, is deficient there is a marked interference with the function of respiration, evidently from oxygen-starvation.

The production or deposition of fat in the tissues seems to be favored by anæmia, especially by achromatosis, probably because the deficiency of oxygen in the blood leads to imperfect oxidation in the tissues. Hence chlorotic girls are often fat. It is said, too, that breeders of fat cattle are, or used to be, in the habit of bleeding the cattle before beginning the fattening process.

The effects produced by anæmia on the circulation are more complicated. The heart is weak and usually rapid, its action often violent. Certain peculiar "murmurs" are produced in the heart, or arteries, or veins, the cause of which is still obscure.

Such a murmur is most constantly heard in the jugular vein above the clavicle, especially on the right side. There is a vibration which may be, when well marked, felt by the finger, as well as heard with the stethoscope. The vibration of the venous wall is even, in extreme cases, visible. The sound has a peculiar whizzing, sometimes musical, character, and is continuous, not pulsating. The explanation of the sound is that an eddy is formed in the blood—the so-called *vena contracta*—as the blood passes from the comparatively narrow jugular vein into a more dilated channel below the clavicle, and that the anatomical arrangements of the part prevent the vein from collapsing. It is sometimes heard in perfectly healthy persons, but is more frequent and louder in anæmia. The cause of its predominance in anæmic conditions is variously explained, but can depend upon only one of two causes—either the diminished volume of the blood, or its lowered density. The former is the more probable explanation. The curious name given to this sound, "bruit de diable," refers to nothing more formidable than a certain toy.

Another anæmic murmur is a systolic one, heard in the second or third intercostal space, just to the left of the sternum. This is often, if not constantly, associated with the dilatation of the left auricle. It has been generally referred to the pulmonary artery, but its real origin is still a subject of controversy.

Besides these, which are the most frequent, a systolic apical murmur is sometimes heard in anæmic persons, and sometimes systolic murmurs over the arota and the larger arteries. The explanation of these is still somewhat obscure, and would lead us too far into cardiac pathology.

In anæmia of young persons, especially in chlorosis, dilatation of the heart is very frequently observed.

Anæmic murmurs have been heard over the hearts of animals experimentally bled to death.

CHAPTER XXVII.

VARIATIONS IN THE WHITE CORPUSCLES AND OTHER ELEMENTS.

The number of leucocytes in the blood is diminished in most anæmic conditions, concurrently with the diminution in the colored corpuscles. There is no recognizable condition in which the colorless corpuscles alone are diminished in number.

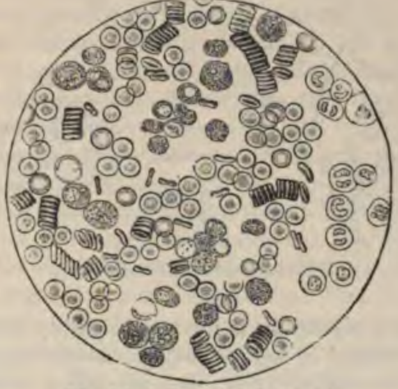
An increase of these corpuscles is met with in several different conditions. There is a physiological increase observed after food is taken, which evidently depends upon an increased supply of lymphatic corpuscles, and is transitory. An increase is also found in pregnancy, in the earlier stages of inflammation, and in some distinct diseases, as pyæmia, tuberculosis, and, it is said, in intermittent fevers. In most of these conditions there is enlargement of the spleen, but, on the other hand, swelling of the spleen may occur without any increase of leucocytes in the blood.

An increase of leucocytes, in proportion to the colored corpuscles, is also observed after copious hemorrhages, apparently because the leucocytes, from their small density and adhesive properties, do not leave the vessels so rapidly, even in proportion to their number, as the other corpuscles, and because hemorrhage is followed by a very copious supply of lymph to the blood by the ductus thoracicus. In cholera, when the fluid part of the blood is rapidly diminished, there is, in consequence, a relative increase of leucocytes.

The above conditions are essentially transitory, and may be conveniently called by the general name of ***leucocytosis***, implying a slight increase only in the number of leucocytes.

In striking contrast to the alteration just mentioned is that in which the number of leucocytes is enormously and permanently increased, which constitutes, in fact, a distinct disease, known as *leukæmia* or *leucocythæmia*. In this condition the proportion of leucocytes to colored corpuscles, which is normally about 1 in 600 or 1200, is increased to 1 in 20 or 30, or even, in extreme cases, to 1 in 3, or even, it is said, more than colored. This remarkable abundance of leucocytes alters the appearance of the blood, which, in slight cases, is of a pinkish cream color, but may almost resemble pus when the change is still more pronounced; so that the condition was once spoken of as "suppuration of the blood." The leucocytes are at the same time somewhat altered in their properties. They do not exhibit any amœboid movements, as was observed by Dr. Cavafy and Dr. Bastian some years ago. They would also appear to have lost the faculty of organization. A case observed by the author some years ago illustrates the latter peculiarity. An elderly man was admitted into hospital with a simple transverse fracture of the femur. There was much swelling, but no evidence of repair, and in the end the patient died of exhaustion. At the post-mortem examination the broken ends of bone were found not united, and surrounded by a large quantity of blood with all the characters of leukæmia, in which there was no organization and no attempt at repair, with scarcely any sign even of inflammation in the ordinary sense of the word. The examination of the rest of the body showed that it was a case of advanced leukæmia.

FIG. 68.



Blood in leukæmia (SCHEUBE).

The colored corpuscles in leukæmic blood are always much diminished absolutely, not merely in proportion to the leucocytes; and, further, there is found to be a marked reduction in the amount of hæmoglobin, even in one case to one-third of the normal, so that there is virtually a condition of anæmia also present.

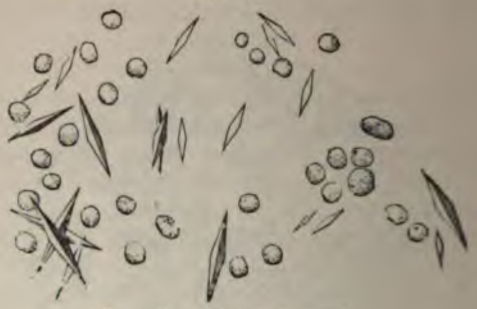
In certain cases the blood is found to contain colored nucleated corpuscles, like those which are found in embryonic blood and also in certain conditions of the medulla of bones—a fact which, as shown by Neumann, has an important bearing on the pathology of the disease.

Besides these changes in the elements of the blood, important alterations are found in the plasma. The proportion of water is in most cases increased, even to 854 and 881 parts per thousand, the density of the defibrinated blood sinking to 1041 or 1036.

Certain peculiar substances have also been found in leukæmic blood—viz., hypoxanthine, lactic acid, and an albuminoid substance much resembling, though apparently not identical with, gelatine. The two former substances are not unknown in other diseases, and possibly occur in healthy blood, though not in the same proportion as in the disease now spoken of.

To Charcot is due the discovery in the blood, spleen, and liver of leukæmic patients of certain peculiar microscopic octahedral crystals which appear to have a constant relation to the disease. They do not appear in fresh blood, but are formed soon after death. Other observers have seen them form within the substance of the leucocytes.

Fig. 69.



Charcot's crystals (Scheube).

Their chemical composition is not yet certainly established. Charcot was at first inclined to regard them as consisting of an albuminoid substance in the crystalline form; but, according to more recent investigations, they are thought to be the phosphate of a peculiar alkaloid which has been obtained also from the semen.

Pathology of Leukæmia.—The exact nature of the process by which the extraordinary accumulation of leucocytes in the blood of this disease is produced has not yet been adequately explained.

It is natural to suppose that there must be an increased production of these corpuscles from the organs which normally supply them to the blood. The organs which are believed to have this function are especially the spleen and the lymphatic glands; but also, as has been more lately shown, the red medulla of bones, and perhaps the smaller masses of lymphatic tissue found in the substance of many organs, as, for instance, in the submucous tissue of the intestinal tract. There is no doubt that some or all of these organs are enlarged in leukæmia.

The spleen is most constantly affected. It is nearly, if not quite always, considerably enlarged, sometimes weighing several pounds. The enlargement is found to be due to a general hypertrophy of the splenic pulp, the Malphigian corpuscles being little if at all affected, and is, in this part, due to an enormous increase of the lymphatic cells.

The distribution of the morbid changes strongly supports the view that an increased number of leucocytes enter the blood from the spleen, since the pulp stands in direct relation with the veins, and is most probably the normal birthplace of the colorless corpuscles.

On the supposition that the changes in the spleen are primary, that form of disease in which this organ is chiefly affected has been called splenic leukæmia. It is the commonest form.

The lymphatic glands are also frequently enlarged, generally along with the spleen, but in rare cases the lymphatic enlargement is the only or the chief one. Since the lymphatic glands also supply lymph-corpuscles to the lymphatic vessels, and thence to the blood, this also may be recognized as a source of the excessive production of leucocytes, and this has been distinguished as the *lymphatic* form of leukæmia. But this form, originally described by Virchow, is extremely rare.

The red medulla of the bones is also affected in some cases, the colorless cells being greatly increased in number, the other parts being diminished. This change has been found, in one or two well-marked cases, without any enlargement of the spleen or lymphatic glands. Hence the conclusion has been drawn that this tissue also is a source of the increased production of leucocytes, and this condition has been distinguished as *myelogenic leukæmia*. The red medulla is in these cases altered in appearance, being grayish-red or yellowish.

There is no proof that this tissue normally furnishes new leucocytes to the blood, but it has been made probable by Neumann that it is the place where leucocytes become transformed into colored corpuscles.

Besides these organs, it has been asserted that the lymphatic follicles of the intestine may, by their enlargement, furnish an excessive number of leucocytes to the blood, and this constitutes an *intestinal* form of leukæmia. But this, as an isolated condition, has been observed in one case only, described by M. Béhier.

In addition to these changes in the lymphatic and blood-forming organs, there is another very constant change in various parts of the body, namely, the accumulation of leucocytes in the interstitial connective-tissue. This is more especially seen in the liver and kidney, but also in other organs. The ordinary fibrous connective-tissue may, no doubt, normally contain a variable number of free or migratory corpuscles, but not at all the proportion in which they are found in this disease, and it is the most noticeable as it occurs in the kidney, where the normal connective-tissue is so scanty as to be scarcely perceptible. It constitutes, in fact, a *cytogenous* connective-tissue.

There can be little doubt that these formations of cytogenous tissue are to be considered secondary, and a consequence of the condition of the blood. The changes in the spleen, lymphatic glands, and osseous medulla mentioned above are, on the other hand, usually regarded as primary, and the cause of the alteration in the blood. Nevertheless, this is far from being absolutely proved, and many recent authorities regard them also as secondary.

If the changes last mentioned are not the cause of the accumulation of leucocytes in the blood, what explanation can be given of this accumulation.

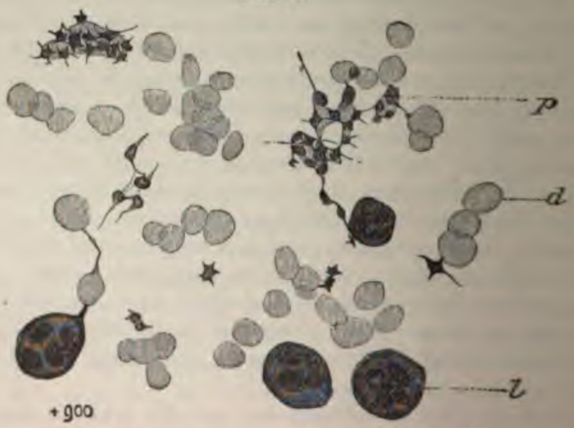
The only other theory is that proposed by Virchow, namely, that the abundance of leucocytes depends on their not undergoing their normal transformation into colored corpuscles, it being assumed that such a transformation regularly takes place in normal conditions. This view is supported by the occurrence of colored nucleated corpuscles already mentioned, and, on the whole, this explanation of leukæmia seems best to accord with the facts.

We have, in this view, to regard the leucocytes in this disease as abortive corpuscles, which have stopped short at a certain stage of development, and on this account are not removed by the constant waste of colored corpuscles which takes place in normal conditions.

Looking on the blood as an organ, the accumulation of leucocytes in it may be regarded as equivalent to a lymphatic tumor of the blood.

Blood-plaques, Blutplattchen, Hæmatoblasts.—It has been known for some years that the blood contains a third kind of corpuscular elements, besides the red disks and the leucocytes. These are minute colorless disks, measuring from 1.5_{μ} to 3.5_{μ} on an average, but with considerable variation in size. They have been often overlooked because they are not clearly seen except with a very high power, and because they rapidly alter when the blood is removed from the body. They are very viscid bodies, and readily run together into granular-looking masses, known as "Schultze's granular masses," which were formerly thought to show disintegration of leucocytes. By very rapid drying of a thin layer of blood however, or by allowing the drop to escape into a 75 per cent. salt solution, this may be prevented, and the plaques observed in a separate form. They are best seen when stained with solution of methyl-violet, or the solution of salt may be tinged with the same dye. When perfectly fresh they are circular disks, but quickly become somewhat angular in shape, as seen in Fig. 70.

FIG. 70.



Blood-plaques as seen in a dried film of blood.

l, leucocytes; *d*, red corpuscles; *p*, blood-plaques (colored with methyl-violet and magnified 900 diameters).

It has been supposed that they are formed only after the blood is withdrawn from the vessels, but by special methods it has been possible to see them in the circulating blood within the vessels, and there can now be no doubt that they are original and normal constituents of blood.

The supposed physiological functions of these bodies can be only briefly referred to here. Hayem, who first accurately described them, regarded them as a preliminary stage in the formation of the red blood-corpuscles, and hence gave them the name of *Hæmatoblasts.*

Bizzozero, who was the first to see them in circulating blood, regarded them as the essential agents in coagulation, and ascribed to them a special importance in the formation of thrombi, more particularly of white thrombi (see page 60), but this is not universally admitted. In the coagulation of a drop of blood, as seen under the microscope, the fibrinous threads certainly appear to start from, or at least to become attached to, the blood-plaques, which at the same time alter in shape, becoming angular. But it is possible that there is some fallacy here, and that the changes in the plaques and coagulation of fibrin may be merely simultaneous.

Pathological Relations of Blood-plaques.—The only known relation of blood-plaques to pathological processes is their assumed connection with thrombosis. Their numbers vary greatly under different circumstances and in different individuals, but the connection of these variations with any special pathological states is at present somewhat uncertain. The average number present in the standard volume—one cubic millimetre—of healthy blood has been placed by two different observers (Hayem and Afanassiew) at nearly the same figure, 200,000 to 300,000 or an average of 250,000, but the numbers show enormous variations; for instance, in enteric fever one patient showed 87,000, another 415,000. Determinations of the relative frequency in different diseases have given the most discordant results. For instance, some observers have found the plaques increased in inflammatory diseases, some diminished, and there is an equally marked discrepancy in observations on the blood in anæmia and leukæmia. There is a more general agreement that they are increased in pulmonary phthisis and, perhaps, other wasting diseases. But the fallacies of observation, caused by the viscidity of the plaques, are so serious that such generalizations have as yet little value. A rough notion of the relative frequency of these elements may be obtained from films of blood dried on cover-glasses. In a number of observations made by this method, I have found no constant relation between the abundance of plaques and any special diseases, but the largest numbers I have seen have been in the blood of phthisical patients.

The subject is, however, well worthy of further investigation, and it is with the object of drawing attention to it, rather than of recording any positive results, that these observations have been introduced.[1]

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[1] In addition to the references given above (p. 61), the following memoirs may be consulted: Hayem, Archives de Physiologie, 1878; Bizzozero, Virchow's Archiv, vol. xc.; Afanassiew, Deutsches Archiv für klin. Med., vol. xxxv., 1884.

CHAPTER XXVIII.

VARIATIONS IN THE PLASMA OF THE BLOOD.

Variations in Fibrin.—The amount of fibrin formed by the blood when it coagulates out of the body varies greatly in different diseases and conditions.

In the days when venesection furnished abundant specimens, it was carefully investigated by Andral, by Becquerel and Rodier, and others.

The proportion of fibrin in healthy blood is from 2.2 to 2.8 parts per 1000 for venous blood, and somewhat more for arterial (Gamgee).

This amount may be increased in disease to as much as 10 parts per 1000. It is increased in certain physiological conditions—viz., in the later stages of pregnancy, and by animal diet. The proportion is small in infants, but increases at puberty. It is not greater in plethoric individuals, but is increased in some cases of chlorotic anæmia.

The most remarkable increase of fibrin is found in acute organic inflammations, such as pneumonia, pleurisy, bronchitis, peritonitis, erysipelas, cystitis, acute rheumatism, inflammation of lymphatic glands, etc. Thus, in acute rheumatism, it has been found to amount to as much as 10 parts per 1000, and in no case observed by Andral and Gavarret was it less than 4, giving an average of from 7 to 8 parts; and in pneumonia both the extreme limits and the average were found nearly the same. It is remarkable that copious blood-letting did not diminish the amount of fibrin, but even seemed, in some cases, to increase it.

On the other hand, in the specific fevers—such as typhoid or other continued fevers, smallpox, scarlatina, measles—the amount of fibrin was never found increased, and in some cases was even diminished. Thus there were cases of typhoid in which the fibrin never exceeded 2.3 and sometimes fell as low as 1 part in 1000; and in smallpox the figures were only rarely higher and sometimes showed as low a minimum. It is remarkable, however, that if in these affections an acute inflammation of any organ supervened, such as bronchitis, or glandular inflammations, or even an eruption of furuncles, the amount of fibrin was increased. In intermittent fevers (ague) the same absence of any increase in the fibrin was noted.

In those inflammatory conditions in which the fibrin is increased a remarkable appearance is often presented by the blood drawn from a vein. The fibrin, together with the leucocytes, rises to the top of the bleeding-basin, forming a layer known as the "buffy coat," while the red corpuscles sink to the bottom of the serum. If the buffy layer contracts very much, the upper surface will become concave, so that the whole resembles a cup; and the blood in this condition is said to be "cupped and buffed." Great importance was at one time attached to this curious phenomenon, as it was supposed to be a special sign of the existence of inflammation. It seems to depend chiefly upon the abundance of fibrin, and hence is seen in acute organic inflammations.

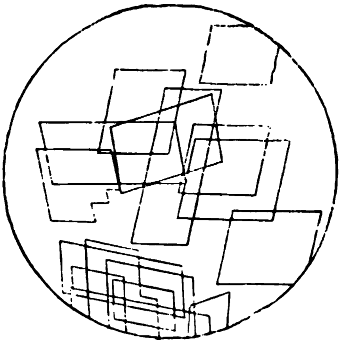
Conditions in which Fibrin is Diminished.—A diminution of fibrin, besides being found in certain cases in specific fevers, as already mentioned, has been observed in organic heart-diseases in their last stage, in malarial cachexia, in scurvy, and in chronic mercurial poisoning.

Fibrin, as seen in coagulated blood, shows some variations in consistence. It is sometimes very firm and elastic, sometimes looser and more friable. The latter quality appears greatly to depend upon a larger proportion of corpuscles being contained in the clot, but not entirely, since the fibrinous threads themselves are sometimes more granular. The cause of these variations has not been clearly ascertained.

Causes of Variations in Fibrin.—While the physiological explanation of the formation of fibrin is still incomplete, we cannot expect to have an adequate explanation of the pathological variations. But if we adopt the theory of Schmidt, that fibrin is formed by the union of two constituents of the plasma—fibrinogen and paraglobulin—under the influence of a ferment derived from the white corpuscles, these variations might, theoretically, be due to variations in any of these. But there is most probability in the hypothesis that the variations in the number of leucocytes which furnish the ferment are the chief determining cause, since these corpuscles are decidedly increased in the inflammatory conditions in which there is an excess of fibrin.

Variations in other Constituents of the Blood: Fats.—The amount of fat normally present in healthy blood is from 1 to 3.3 parts per 1000. When this proportion is much increased, the serum presents a milky appearance, like chyle, and is called chylous serum. The name lipæmia is also given to this condition.

FIG. 71.



Plates of cholesterin.

A chylous condition of the serum is found to occur normally after abundant ingestion of food, especially such as contains fatty matters. It is also stated to be found in chronic alcoholism, in Bright's disease, and in certain acute diseases, such as pneumonia, acute rheumatism, and hepatitis. But these statements require confirmation. More certain results have been obtained in diabetes. In this disease the serum of blood has been found milky, from the presence of notable quantities of fat soluble in ether. The fatty globules may also be seen with the microscope, and recognized by staining with osmic acid. In one case Gamgee found 10.8 parts of fatty matters, and 1.96 of cholesterin per thousand, in blood drawn during life. This is not, however, found in all cases of diabetes.

The proportion of cholesterin is also stated to be increased in acute febrile diseases, acute inflammations, and especially in certain cases of jaundice.

Sugar.—There is, according to Pavy, a small quantity of glucose normally present in blood, which was found to be, in the blood of the dog, on the average. 9 parts per 1000.

In diabetes this proportion is enormously increased, amounting, in certain cases, to from 4.97 to 5.76 parts per 1000.

Urea and Uric Acid.—The amount of urea present in normal blood varies from 0.2 to 0.4 part per 1000.

This proportion is largely increased in Bright's disease, in cholera and in yellow fever, and also, it is said, in diabetes and febrile affections.

In Bright's disease 0.4 to 0.6 part in 1000, and even more, has been found. This excess constitutes the condition known as uræmia, but the so-called uræmic symptoms, such as coma and convulsions, cannot be due to this cause alone, but in part also to the hydræmic condition, and perhaps partly to some other poisonous principles which may accumulate in the blood.

In cholera 2.43 and 3.6 parts per thousand respectively have been found in two cases.

Uric Acid is present in normal blood in extremely minute quantities. In gout, both during the acute attacks of the disease and in the chronic condition, it is present in notable quantities, and may be obtained by crystallization from the serum. It may also be shown in the serum obtained from a blister.

The name lithæmia has been given to the condition of excess of uric acid in the blood. It was attributed by Murchison especially to defective action of the liver, and regarded as the condition antecedent to gout.

Salts.—Nothing definite is known about the variations in the salts of the blood in diseases. In hydræmic conditions the proportion of salts in the serum is necessarily diminished, and in cholera, when the amount of water is diminished, the salts must be relatively increased.

Pigment.—In chronic conditions of malarial poisoning, after repeated attacks of ague (the malarial cachexia), the blood may contain black or brownish pigment-granules, partly free, partly contained in the leucocytes. It is altered blood-pigment, which passes into the blood from the spleen, where it has accumulated in consequence of repeated hemorrhages in that organ, and may be thus distributed to other parts.

Gases of the Blood.—Although it is probable that in certain conditions *e. g.*, anæmia or oligocythæmia, the amount of oxygen in the blood is diminished, and in conditions of imperfect respiration the amount of carbonic acid increased, no precise determinations have been made of these variations.

In the blood of patients with the plague, free sulphuretted hydrogen was found by the French pathologists in Egypt.

Parasites of the Blood.—The parasitic organisms, animal and vegetable, which are occasionally met with in the blood, will be described in the second part of this work.

PART II.

THE CAUSES OF DISEASE.

CHAPTER XXIX.

MECHANICAL AND PHYSICAL INJURIES.

In entering upon the general topic of Causes of Disease, which is the subject of the second part of this work, it is necessary at the outset strictly to limit the extent to which it will be possible to range over this wide field. It will be only practicable to consider that class of causes of disease called Injuries; the word being taken in a wide sense, so as to include, (1) injuries from mechanical and physical causes; (2) injuries from poisons; (3) injuries from living things in or upon the body.

Mechanical Injuries.—A full discussion of the injuries caused by mechanical violence would be evidently quite out of place here, since it would extend over a great part of the field of surgery.

The consequences of mechanical injury may be regarded as *special* and as *general*. The special consequences are such as removal, severance, or destruction of organs or other important parts. The general are such as are produced in all tissues alike. Now it is plain that such special consequences of mechanical violence as fractures of bone, division of nerves or arteries, or rupture of internal organs do not come under consideration in General Pathology. But there are certain universal consequences of all mechanical injuries whatever parts they may affect, and these admit of being stated in a general expression.

In all wounds or mechanical lesions, a certain proportion of tissue composed of cells and other elements is killed or destroyed. The amount of destruction thus produced is not necessarily in proportion to the gravity of the injury in other respects. A clean wound with a sharp weapon may cause death by dividing a vital part while producing a minimum of tissue destruction; while, on the other hand, a crushing or bruising wound may kill a considerable mass of tissue without producing any serious effect on the body as a whole. But in all cases there is some tissue-death, which is what the general pathology of injury is concerned with, especially since, as will be seen hereafter, an effect essentially the same is produced by other injuries.

The further results which follow on the death of elements or tis
are twofold. In the first place, the dead material is injurious

body, as generating noxious substances which are absorbed, and because it serves as a nidus for the growth of organisms which are still more deleterious. In the second place, the destroyed parts have to be restored, so that new-growth, in healthy conditions, always follows mechanical injury. Till the dead matters are absorbed or eliminated, and the part restored, so far as restoration is possible, the effects of the injury are not compensated. The processes of elimination and repair have already been spoken of in treating of inflammation.

There is further one general or somatic effect of severe mechanical injury which must be briefly referred to, namely, the condition called Shock. The symptoms of shock are so fully described in surgical works that it will be only necessary to say here that failure of the heart, a toneless state of the arteries, failure of respiration often with cyanosis, lowered body-temperature, and prostration of the intellectual and sensory functions of the brain, are the most important. Injury is admitted to be the chief cause of shock. "As a rule, the more extensive the injury, the nearer it is to the centre, and the more it assumes a crushing character, the greater will prove the amount of shock. The crushing of a finger or bruising of a testicle often occasions severe shock; so also do extensive burns or scalds" (MacCormac).

There can be little doubt that the effect producing shock acts through the nervous system. Intense pain may produce it, though it may also occur in severe operations even under anæsthetics. Moreover the same condition may result from an intense mental impression or emotion, whether of terror, excitement, or grief, such as witnessing the death of others or even severe accidents, which have, in some instances, given rise to fatal shocks in the bystanders.

Physical Injuries.—The injurious effects of the physical agents heat, cold, and electricity must be briefly considered.

General Effects of Heat.—A very high external temperature may be borne by the human body so long as the regulative apparatus is able to keep the body temperature within ordinary limits. Thus in dry air a temperature of 210° or even 260° has been borne for some minutes, and still higher numbers are given. Work may be carried on for some hours at from 120° to 160°; and in the tropics a dry temperature of 120° to 130° is sustained for a long time without damage and with only slight rise of temperature of the body. But when the effects of high temperature are combined with those of fatigue, as in the case of soldiers marching or others, the regulative machinery appears to become suddenly exhausted, with the result of high body temperature (104° or more) and other symptoms of hyperpyrexia, which may be rapidly fatal (see p. 139). This is heat-stroke or heat-apoplexy, which is not necessarily due to the direct rays of the sun, since it often occurs early in the morning and in the shade. The effects of direct solar heat, or sunstroke, appear to be due more to cerebral hyperæmia.

Small animals, such as rabbits, dogs, etc., exposed to a temperature of even 100° to 104° in closed chambers for some hours generally die, and a temperature of 112° has been found constantly fatal under such circumstances. Since muscle-substance contains one albuminous body at least which coagulates at 112°, it is thought that death may be caused by the coagulation of the respiratory muscles and heart. But this hypothesis must not be pressed too closely.

It has already been mentioned that in animals exposed for a long time to a high temperature, parenchymatous (and also fatty) degeneration of muscles and glands is produced. In Litten's experiments exposure to a temperature of 97°–99° for a few days had this result. Similarly the parenchymatous degeneration of organs in febrile diseases has been thought to be a consequence of high body-temperature, but this is not established beyond a doubt.

Local Effects of Heat.—A temperature much above the normal has for its usual result inflammation, or, if still more intense, necrosis (see p. 139). The effects of ardent heat or burning on the tissues, though apparently more complicated, are explicable in the same way. The lowest degree of injury is seen in the production of hyperæmia, which, however, if followed, as it often is, by desquamation, must be considered as a slight form of inflammation. In the next degree is observed the formation of a blister, which means necrosis of the superficial portion of epidermis and rapid inflammatory exudation from the deeper portion. A still more severe injury causes deeper necrosis of the tissue and the formation of an eschar, while in extreme cases the tissue may be actually carbonized. The neighboring parts will naturally pass into the state of inflammation. The injurious effects of burns and scalds depend partly upon the shock caused by injury to superficial nerves; but partly also, it would seem, upon alterations in the blood. In Wertheim's experiments upon animals it was found that the blood after severe burns contained yellowish granular masses resulting from the disintegration of red corpuscles; and hæmaturia, probably also dependent on destruction of blood-corpuscles, always resulted. The appearances after death, when life is prolonged, are ecchymoses on serous and mucous surfaces and parenchymatous degeneration of muscles and glands. Inflammation of the lungs may result and in rare cases ulcers of the duodenum. The latter are probably the outcome of patches of ecchymosis or hemorrhagic infiltration, which I have observed in that situation after burns.

Burns affecting a large portion—it is said more than one-third—of the surface are generally fatal; and sometimes the same result follows a much less considerable lesion.

General Action of Cold.—Exposure to even severe external cold may, as is well known, be borne without damage if the body is in a healthy state. But when the exposure is greatly prolonged, or the body badly nourished, or its temperature not kept up by exercise, a fatal result may ensue. It is not known precisely in what way death is produced, but there is much probability in the view that it is by simply lowering the temperature of the body. Precise observations on this point are, for obvious reasons, not likely to have been made in the human subject, but it is found that in the case of any warm-blooded animal a lowering of the temperature of the body below [illegible] appears to be nearly always fatal. The mode in which death is produced is either by failure of the heart or by anæmia of the brain. The drowsiness which is a well-known symptom of the injurious effects of cold, is probably due to the latter condition.

Action of Cold on Tissues.—Single elements such as leucocytes even of warm-blooded animals may be exposed to a freezing temperature and yet revive, as may also eggs; but in some countries the excessive cold sometimes causes necrosis of exposed parts, such as the nose, ears, and fingers, known as frostbite. The process appears to be that the part is first rendered totally anæmic and then its tissues and the vascular walls are further altered by cold, so that when the blood returns, the vessels are impermeable, and local death of the part takes place. A lower degree of the same change is seen in the common chilblain. The vessels are altered by cold, not sufficiently to render them impermeable but only to produce stagnation of blood with cyanosis, to which, according to well-known principles, is added inflammation. The inflammation however, shows a well-marked tendency to ulceration or necrosis, not to active suppuration. These changes have a close resemblance to the graduated series of effects observed by Cohnheim to be produced in the ears of rabbits when exposed in a bloodless state to extremes of cold and heat.

Effects of Changes of Temperature.—It is a familiar fact that vicissitudes of temperature succeeding one another rapidly, have deleterious consequences, especially in setting up inflammations of internal parts. Although of late years there has been a tendency to ascribe less than was formerly ascribed to these causes, no scepticism can deny the effect of taking cold in producing such complaints as catarrh of the respiratory tract, and muscular rheumatism. The manner in which these effects are produced is far less certain. The most plausible explanation is that of Rosenthal, that disease from cold happens when the skin is very full of blood from exposure to heat or excessive heat-production, and is then cooled rapidly so that there is a great difference between the temperature of the blood in the skin, and that of the blood in internal parts. At the same time the cutaneous vessels contract, and thus masses of cooled blood are thrown in upon the internal organs, of which the lungs are, for obvious reasons, most likely to suffer.

Effects of Electricity.—Death from a stroke of lightning is due to the discharge between the earth and the cloud passing through the human body, which, from the amount of water it contains, is a good conductor. Since death comes without there being necessarily any visible alteration or wound of the body, it is doubtless caused by paralysis of the nerve-centres, as is evidenced by the instantaneous insensibility which accompanies the stroke, even when it is not fatal. The heart and respiratory movements are weakened in non-fatal cases, probably from an affection of the medulla oblongata. The line of discharge through the body may be marked by ecchymoses, or sometimes by ruptures of certain parts; while on the surface the points of extrance and exit are shown by small wounds, sometimes complicated by curious tree-like markings or "lightning figures" caused apparently by the discharge spreading in an irregular manner over the skin. Rapid putrefaction, fluidity of, and production of gas in the blood have also been described as post-mortem appearances, but are of uncertain significance. In many cases the appearances are quite negative.

Of late years the powerful induced currents used for electric lighting have in many instances been fatal to those who have incautiously touched the conductors and thus made the current pass through their bodies. No characteristic changes have been found, this kind of discharge producing less physical commotion than the disruptive discharge of lightning. In one case a small blister was seen upon the finger of a man who was suddenly killed by touching a machine. The histology of this case was carefully examined by Messrs. Shield and Delepine, who found changes in the epidermis and true skin comparable to, though not precisely like those observed in, blisters produced by burning.

CHAPTER XXX.

THE ACTION OF POISONS.

THOUGH it is no part of the scope of this book to enter into the pathology of poisons specially, there are a few broad facts respecting the action of this class of causes of disease which must be considered before we can understand the action of those specific causes which are more important for our purpose.

Poisons are defined as "substances which are capable of seriously affecting health, or destroying life," usually through being absorbed into the blood, but sometimes by a very violent action on some part of the body.

A pathological definition of poisons must be wider than this, and would be rather something as follows: "Substances capable of injuring the body, either by causing damage to the tissues or by producing functional disturbance."

Poisons are distinguished by medical jurists into two main classes: (1) Irritant, (2) Neurotic; and which, though a rough classification may answer our present purpose. Irritant poisons include acids, alkalies, metalloids and metals or metallic salts, and some vegetable substances.

The property common to all these substances is that of causing irritation or inflammation of the digestive mucous membrane, with the well-known symptoms of vomiting, purging, etc. They also affect other surfaces, whether broken or intact, in a greater or less degree.

Besides these local symptoms, they produce, when absorbed into the blood, other symptoms, depending upon the way they affect the nervous or other systems of the body. These symptoms are the same, by whatever channel the poison enters, but vary according to the amount absorbed.

Though absorption takes place, generally speaking, more easily from the digestive tract than from any other part, it may take place, under some circumstances, from any part to which the poison is applied.

Irritant and Corrosive Poisons.—When the local action is very violent, corrosive or destructive action is produced and hence certain poisons, such as strong acids, corrosive sublimate, etc., are classified as *corrosives;* but this distinction, though practically important, is, pathologically speaking, only one of degree.

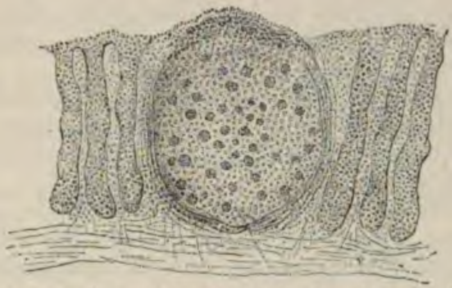
The one local action common to all irritant and corrosive substances is that of producing injury, necrosis, or local death of the tissue-elements, the evidence of which will be different according to the tissues affected. The most conspicuous action, which is regarded as a characteristic sign of irritation, is that exerted on the bloodvessels, leading to hyperæmia, increased exudation of serum, extravasation of the elements of the blood—in fact, the type of vascular inflammation. If the injury to the vessels be very severe, hemorrhage, or extravasation of the blood as a whole, results.

The action of the parenchymatous elements, though less noticed in practice, is not less distinct.

The epithelium of the digestive tract may be killed off in one mass, producing a so-called false membrane or slough, which is really nothing but the necrosed mucous membrane peeling off. This is seen, for instance, as the result of swallowing concentrated mineral acids, corrosive sublimate, chloride of zinc and other corrosives, and also from tartar emetic and phosphorus. In extreme cases a portion of the walls of the stomach may be completely destroyed, causing perforation or laceration. This action goes on after death, if the poison remain in the stomach or intestines. If the poison be more dilute, the necrotic action consists in causing granular (albuminous) degeneration or cloudy swelling of the epithelium, generally accompanied by coagulation of albumen.

This is probably a constant result of the action of metallic poisons, though not always noticed. It may occur without any gross alteration of the mucous membrane visible to the naked eye, or may cause yellowness and opacity of the epithelium (Fig. 72).

FIG 72.



Mucous membrane in acute arsenical poisoning (GROHE and MOSLER).

One lymphatic follicle is shown, with fatty and granular contents beginning to break down at its outer aspect. Also several peptic glands with granular degeneration of the epithelium.

It may be traceable when the signs of vascular inflammation are very slight or absent. In a case of fatal poisoning by antimony which the writer examined some years ago, there was no visible hyperæmia or inflammation of the stomach, but the mucous membrane was found, on microscopical examination, to be completely disorganized, the epithelial elements being converted into granular masses, of which the structure was hardly recognizable. In this case the poison was probably taken in a very dilute form, though in a large dose.

This poisonous action is exerted to a certain extent by the mineral acids, and the salts of a great number of metals, and by certain metalloids such as phosphorus.

Among metallic salts, those of the heavy metals more especially exert a necrotic action.

Alkaline salts, being normally contained in the fluids of the body, are less destructive, but even some of these, in great concentration, cause intense inflammation. The caustic alkalies also dissolve the tissues.

Among the other metallic salts, the action is greatly modified by solubility, quite insoluble substances having, for obvious reasons, only a mechanical action, while nitrates, which are most soluble, are also the most active; soluble chlorides and sulphates coming next, while insoluble or slightly soluble chlorides, carbonates, and oxides have comparatively little necrotic action.

For instance, mercuric nitrate and silver nitrate are powerful caustics; zinc chloride and mercuric chloride also, while soluble sulphates, such as those of copper and zinc, have a similar but much milder action when used in a concentrated form.

There are also great differences, which cannot here be considered, dependent upon the chemical nature of the base. For instance, the mercurous compounds are, even taking into account their inferior solubility, much milder in their action than mercuric salts.

Salts of lead can hardly be used in sufficient concentration to produce an actually destructive effect, but have a local action which greatly resemble that of the above-named salts when much diluted.

Iron salts have generally no local destructive action, except that, in a very concentrated form, they may produce inflammation; but they are poisonous if injected into the blood.

The mineral acids show a similar gradation of locally poisonous effects. Concentrated, they are all powerful corrosives, destructives or caustics. In the case of sulphuric acid this action is aided by its powerful affinity for water.

Nitric acid acts in a very similar manner to the more powerful metallic nitrates. Hydrochloric acid is less destructive than the others. In a more dilute form they produce inflammation.

The stronger organic acids, such as acetic, lactic and oxalic, have a *local* action like that of the mineral, producing corrosive or inflammatory action according to their degree of concentration.

Explanation of Tissue-changes.—The explanation of the above-mentioned facts is doubtless that the salt or acid produces a chemical reaction with the albumen of the tissue elements. These are either killed outright and converted into dead matter which the body throws off, or else partially killed, so that their functions are interferred with, their chemical composition altered, and their physical resistance usually much lowered.

One important difference in the local action of metallic salts depends upon whether they form a soluble or insoluble compound with albumen. In the former case the salt is easily absorbed; in the latter the tissues are hardened and a certain barrier is set against absorption. This property is common to all the heavy metals, and is one cause why they are so slowly absorbed from the digestive canal.

But the action of all metallic salts, except those of the alkalies in a dilute form, is essentially necrotic. The result is either absolute necrosis or the condition of granular parenchymatous degeneration of the tissue-elements. Whether the tissues swell or contract depends largely upon whether they are freely supplied with water. Many salts and acids withdraw water from the tissues, and hence contract their bulk.

The bloodvessels may be primarily or secondarily affected. Primarily they, more especially the capillaries, suffer damage, like the tissue-elements; hence, increased permeability, exudation, emigration of leucocytes, etc., and probably, in some degree, dilatation. Few metallic salts possess the power of causing contraction of the vessels, not even those which we regard as astringents, except salts of lead and silver (Brunton). Secondarily the vessels are affected by the damage done to the tissues, which lowers their elasticity and hence affects the circulation in the capillaries, as before explained.

Apparent Exception.—When corrosive or any locally destructive substances are applied to the tissues in a dilute form, the above-mentioned effects will seem to be wanting, or even the opposite to be produced. Dilute solutions of metallic salts are what we call astringents, so that, whether the action is corrosive, irritant, or astringent, is in many cases only a question of degree. Astringents contract the bulk of the tissue-elements, harden their substance, and thus increase the resistance of the tissues. By this they remove congestion in the capillaries and thus act as the cure of inflammation. Lead and silver salts also limit the supply of blood by contracting the vessels.

These facts do not contradict what was stated above. They only show what happens if the action of destructive substances be carefully graduated so that no actual destruction occurs. Caustic alkalies, however diluted, never act as astringents, because they have a solvent, not a hardening, effect on the tissues.

The action of metallic astringents on the tissues is, especially in the case of lead and silver salts, very similar to that of cold.

Absorption of Poisons.—The poison, or other chemical substance, applied to an external or internal surface of the body may be generally regarded as divided into two portions. One is left on the surface and thrown off, the other absorbed. Some substances are scarcely, or not at all, absorbed, even by the intestines. A few only are absorbed by the skin. But if absorbed, by whatever channel, they will in the end be taken up by the blood and carried all over the body.

In all cases the powers of absorption are limited, so that if a large portion of the poison be applied to the surface, a small portion of it only may enter the circulation. But if the poison be completely soluble, given in a dilute form and in small quantity, the whole may pass into the blood and none be left on the surface where it entered.

The amount of absorption will vary indefinitely, according to the solubility of the poison to its diffusive power—bodies with a high atomic weight being generally less absorbable than those of low atomic weight—and so on. These variations need not here be considered.

Secondary Effects.—When a poison has once entered the blood and is distributed to the various organs and tissues, it will affect them in various ways.

A large part of the effects will be *functional;* that is, will depend upon a chemical reaction between the poison and the tissue-elements in which the latter preserve their vitality. For instance, zinc and antimony salts, by their action on the nerve-centres, independently of local action on the stomach, will cause vomiting. Arsenic may produce certain kinds of paralysis, and lead other kinds. Many metallic salts affect the innervation of the heart, producing cardiac paralysis or fatal syncope. Oxalic acid may, under different circumstances, affect the heart, causing fatal collapse and syncope, the spinal cord, causing tetanic symptoms, or the brain, causing coma. Copper salts, besides other symptoms, may produce "dilatation of the pupils with stupor, coma, tetanus, or paralysis." Mercurial salts produce salivation; and, rarely, sulphuric acid has produced the same symptoms. Even iron salts are functional poisons if introduced into the blood. These instances might be multiplied indefinitely. It should only be remembered that there is something specific in the action of most poisons, affecting certain tissues especially, others other tissues, doubtless in consequence of their different chemical composition. But generally, salts of all the heavy metals have a poisonous action on muscles, nerves, nerve-centres, and glands (Brunton).

The important points to remember in connection with them are: (1) that these secondary effects of the poison are the same by whatever channel the poison is absorbed, whether by the mouth, by injection into the veins, or otherwise. (2) They are produced by direct contact of the poison contained in the blood with the affected organs, the only other possible explanation—viz., that of reflex action from the irritated mucous membrane—applying only to a small proportion of symptoms. (3) The quantity of poison in contact with the affected organs must be comparatively very small, since the amount absorbed is diluted with the whole mass of the blood. (4) The nervous system, and especially the nerve-centres, appear to be the parts earliest affected, because they consist of the most sensitive and easily disturbed protoplasm. (5) If the dose be not too large, and be completely eliminated, the symptoms subside, and the parts affected appear, in non-fatal cases, to be left in an uninjured condition. This, however, is a question of degree, as will be obvious from what will be said presently.

The only objection to this generalization is that alluded to above, namely, that large quantities of irritant poisons introduced into the stomach give a shock to the nerves which by reflex action through the nerve-centres accounts for some of the symptoms of neurotic disturbance. The effect is similar to that of a violent blow on the epigastrium or of an electric shock. But this only applies to very large doses, and obviously does not account for the effects of poisons introduced into the blood.

Tissue-changes Produced by Absorbed Poisons.—If the dose of poison be very large, or if from continued absorption a large quantity be circulating in the blood, it will produce, in various parts, changes similar to those produced by direct application to the surface of absorption. These changes have been little studied except in certain cases, but are probably much more general than is supposed.

Sulphuric acid is an instance. This poison absorbed into the blood, even in quantity insufficient to give it an acid reaction, produces fatty degeneration of the liver and striated muscles, especially the heart. The effects on the kidneys, by which the acid is eliminated, are still more marked. I have seen parenchymatous degeneration of the kidney epithelium. German pathologists have described this in many cases and also commencing interstitial inflammation. Phosphoric acid produces the same changes; other mineral acids, it is said, in a less marked degree.

Phosphorus-poisoning leads to extreme fatty degeneration of the liver, a similar condition of the kidney epithelium, and also of the voluntary muscles and heart.

In acute arsenic-poisoning there is fatty degeneration of the liver, kidneys, muscles, and heart. In protracted cases the fat disappears and atrophy of the epithelium of the glandular organs is observed.

Antimony, in chronic poisoning or where life is sustained for some days, produces fatty degeneration of the liver and kidneys; in fact, the same changes as in the mucous membrane of the stomach. It has also been shown that arsenic and antimony, if injected into the blood, are excreted partly by the stomach and intestines, and sometimes produce in them irritative lesions like those set up by the primary application.

In lead-poisoning I saw in one case extreme granular parenchymatous degeneration of the renal epithelium without any interstitial inflammation, and was therefore inclined to attribute the kidney-inflammation to some other cause than to lead. However, MM. Charcot and Gombault have shown that in experimental poisoning of animals by lead salts, the epithelium of the kidney is first affected with granular degeneration, and that interstitial inflammation occurs subsequently. The common result (being the final stage) of chronic lead-poisoning is interstitial nephritis.

Cantharides is a poison producing intense local inflammation of the skin, starting with complete necrosis and exfoliation of epidermis (blister). When absorbed into the blood, the poison is eliminated by the kidneys, producing inflammation there. It has also been shown by Cornil and Ranvier that subcutaneous injection of cantharidine produces inflammation of the trachea and air-passages. In these, as well as in the kidneys, the first effect of the poison is seen in swelling, with granular degeneration, of the epithelial structures, accompanied or followed by inflammatory hyperæmia from injury to the vessels and connective tissues.

All salts of the heavy metals, if introduced into the blood, produce similar changes in the kidneys when eliminated through them, though in various degrees.

These examples show that the action of irritant poisons on all tissues is essentially the same, though, of course, weaker where diluted with blood than where applied in a concentrated form.

This action is, broadly speaking, necrotic or destructive, though it may, in the first instance, be merely a disturbance of the nutritive activity of the cell, as distinguished from its functional activity. Thus, for example, fatty change from phosphorus or other poisoning, has been ascribed to impeded oxidation or respiration of the cell; but its final result is atrophy or necrosis.

Neurotic Poisons.—These poisons include the classes distinguished by Taylor as cerebral, spinal, cerebro-spinal, and cerebro-cardiac.

They have, for the most part, no local irritant action (though in one group, the narcotico-acrids, this action is not wanting), but when absorbed produce effects which are most marked in the nervous system.

Speaking broadly, these poisons are mostly chemical compounds containing nitrogen, and might be arranged in a series of increasing complexity, starting from hydrocyanic acid, HCN, as the lowest term of the series. A great many are alkaloids or compound ammonia bases. The only important group of narcotic poisons not containing nitrogen, includes those derived from the alcohol and ether series.

These poisons are for the most part readily absorbed by the stomach and also when applied to other mucous surfaces, or injected into the subcutaneous cellular tissue, or into the blood.

The changes produced at the part where the poison enters the body are slight or unimportant; but in whatever way introduced they exert the same action on other parts of the body.

This action is seen primarily in the nervous system. Each poison seems to have a power of selection by which it affects one or more parts of this system—the brain, the medulla oblongata, the spinal cord, the ganglionic system, or, more rarely, the peripheral nerve terminations.

This apparent selective power must essentially consist in a reaction between the poison and the nervous tissue, and therefore depends upon the chemical constitution of both these factors.

According to these variations, neurotic poisons have been classified —*e.g.*, by Taylor, as follows: *cerebral*, such as opium and its alkaloids, and others, which affect the brain, producing stupor and coma generally without convulsions. *Spinal* poisons, which affect the spinal cord, producing convulsions, either clonic or tetanic. Strychnia is the chief member of this class. *Cerebro-spinal* poisons, which act both on the brain and the spinal cord, producing such symptoms as delirium, convulsions, coma, and paralysis. Instances are atropia conia, aconitia, etc. The nerves of sensation and motion may also be affected by these poisons.

Cardiac or *cerebro-cardiac* poisons are those which affect the action of the heart. This effect may be produced, through the pneumogastric nerve, from the brain, or by affecting the intrinsic cardiac ganglia. Digitalis, tobacco, Calabar bean belong to this class: and also muscarin. Woorare has an action special to itself, paralyzing the muscles by affecting the terminations of the motor nerves in them.

These distinctions must not be taken too absolutely, since different organisms are differently affected by the same poison. For instance, opium frequently causes convulsions in children, though rarely in adults; and in the lower animals, where the cerebrum is little developed, as in frogs, the chief effect of the opium alkaloids is on the spinal cord, producing convulsions or tetanic spasm.

The above instances are enough to show the action of neurotic poisons on the nervous system. It remains to consider whether their action is limited to these parts.

General Action of Neurotic Poisons.—The fact appears to be that the nervous tissues are first and chiefly affected, in virtue of the susceptibility of their protoplasm, but that if death be not produced, and the action of the poison be intense and long continued enough, other parts are also affected.

The next, perhaps, in order of susceptibility appear to be the secreting glands. In profound opium-narcosis, almost all the secretions appear to be arrested; the glands being, in fact, put to sleep. The sweat-glands form an exception, being apparently specially affected by the condition of the nervous system. Opium, again, has been found to produce, in invertebrate animals, weakening of the contracile tissue and consequent paralysis of movement. It has even been said that opium affects the contractile movement of sensitive plants, but the results appear to be ambiguous.

From these and other facts we may conclude tentatively that the action of opium (and probably other neurotics also) is one affecting protoplasm generally, though the effect on other than the nervous tissues is so slight as to pass unnoticed. In man the chief effect is on the brain, in consequence of the great development of that organ; in the lower vertebrata on the spinal cord and ganglionic system; in the invertebrata on the tissues generally. Dr. Lauder Brunton gives many facts showing the functional effect of drugs on protoplasm. Quinine has the most marked effect in checking the protoplasmic movements of amœbæ, and similar "amœboid" movements of leucocytes.

The essential point is, that the action of neurotics is functional, not affecting the structure of the tissues. On this basis we might rather classify poisons, for our present purpose, as (1) *tissue poisons*, which damage or destroy the structure of the tissue-elements, including all the corrosive and so-called irritant substances; (2) *functional poisons*, which disturb the function of elements without damaging their substance, *i. e.*, neurotic poisons so-called. But as the greater includes the less, the first class of substances, when acting feebly or in a small dose, will produce functional disturbance. But the converse is not true, even the most intense functional disturbance, if transitory, being possible without damage to the tissues.

What Poisons do not Effect.—One extremely important negative law should be borne in mind. 1. No unorganized poison, such as has been described, is capable of directly producing the condition called fever. The temperature of the body, if affected, is lowered, and may be lowered in an extreme degree. The few exceptions to this law which are known, serve to test the correctness of the rule.

Irritant poisons, as arsenic, which produce local inflammation may, by so doing, produce fever secondarily, in the same way as other local injuries. This is not a direct result of the poison, but of the inflammation.

In lead-poisoning, when violent colic is produced, the temperature may rise, as a consequence of the violent muscular contractions. In rare cases of fatal belladonna-poisoning, a high temperature has been observed; probably from the action of the poison on the heat-centre in the brain.

The importance of this fact is, that it distinguishes the unorganized, or not living, poisons from the living poisons which cause specific diseases. It often helps diagnosis, and may be broadly regarded as a distinction between poisoning and specific infective disease.[1]

2. Another law, important in the same respect, is that unorganized poisons do not affect the tissues so as to cause overgrowth—that is, they do not produce tumors or inflammatory new-growths, as the poisons of syphilis, tuberculosis, etc., do; their action being, broadly considered, destructive and not stimulating to life. One partial exception to this rule is seen in the action of alkaline bromides, when taken in large quantities for a long time, on the skin. The bromide rash sometimes consists of lumps having a considerable resemblance to inflammatory new-growths, but differing in being essentially transitory.

3. Finally a most important law of poisoning is, that the condition is not transmissible from one person or animal to another, except in so far that the tissues or fluids may contain a certain portion of the poison, and so be, in a limited degree, poisonous. If these three laws are borne in mind, their importance will be seen when we have to speak of other specific kinds of morbific agents.

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[1] Some qualification of this law has been made necessary by the discovery of certain poisonous alkaloids or *ptomaines*, which have the property of producing fever (see below).

CHAPTER XXXI.

FERMENTS AND ANIMAL POISONS.

It will be necessary before going further, to define what we mean by a ferment. This word is used in two senses. First, for a living plant, such as yeast, which sets up the change called fermentation in certain substances, such as sugar. These *living ferments* we put aside for the present.

Secondly. Ferments in the physiological or chemical sense—also called soluble ferments or enzymes—are certain highly complex and easily decomposed organic substances, which, within certain limits of temperature, have the power of decomposing comparatively large quantities of other organic substances in such a way as to form two or more simpler substances. "The sum of the heats of combustion of the products is less than that of the original substance" (Flügge). This amounts to saying that the atoms of the original compound are not only arranged in two groups instead of one, but are brought, on the whole, nearer to one another, so that less energy is liberated by breaking them up. It would follow from this that some energy is liberated by the action of the ferment; and the usual rise of temperature during fermentation shows that this is the case. Generally the elements of water are taken up in the reaction.

So far as is yet known, these substances are only formed by living animals and plants. In the higher animals they are often the product of special glands—for instance, pepsin of the gastric glands, ptyalin of the salivary, etc., but some are also found in the tissues. In the higher plants they are mostly found in seeds or fruits, *e. g.* emulsin in the almond, diastase in barley, etc., though also in other parts. But in lower organisms, animal or vegetable, they appear to be generally distributed through their substance.

Physiologically, ferments are very important, especially in nutrition, their function being to convert food-stuffs into substances more soluble, more diffusible, and thus capable of being absorbed; *e. g.*, conversion of albumen into peptones. Thus in seeds their function is to convert the albumen into substances better adapted for the nourishment of the embryo. But in the animal body many other nutritive processes are performed under the influence of ferments. In plants generally the number and variety of ferments are very great, and the action of many is as yet quite unknown.

Seeing that ferments are thus strictly associated with living organisms, it has been thought that the action of living ferments—yeast, bacteria, etc.—depends upon their producing soluble ferments; but this is not yet sufficiently established, though very probable. In general the action of ferments is limited to one chemical reaction, or may be extended to a similar reaction on allied chemical substances; while the action of living organisms is more complicated and more various. It is most important to remember that the ferment is not increased during the fermentation, but remains unchanged in quantity or is exhausted.

Action of Ferments.—The most notable point in the action of ferments, regarded as a chemical process, is that a very small quantity serves to transform a very large quantity of the substance acted upon and this without apparent change in the ferment.

The proportion which can be thus transformed is, however, not quite unlimited. For instance, diastase is unable to change more than two thousand times its own weight of starch into glucose.

Similar reactions have been in many cases effected by other chemical agents. For instance, starch may be converted into glucose by continued boiling with dilute sulphuric acid, just as by the action of diastase; and albumen may be peptonized by long-continued boiling with water. But the operation is slower in such cases, and requires relatively large quantities of the reagents.

Ferments act within a certain range of temperature, and the maximum effect is often confined within very narrow limits, lying mostly between 110° and 150° F., but there is some action at lower temperatures. The action of most is stopped by a temperature of 150° to 170°. Solution, or at least moisture, is essential to their action. The reaction of the fluid has great influence, but affects different ferments differently. Slight excess of acid is favorable to the action of some, as diastase and invertin. Pepsin acts only when, as in the stomach, a distinct excess of acid is present. But the action of others—*e. g.*, emulsin—is hindered by minute quantities of acid, and great excess of acid is always injurious. Even a slight excess of alkaline reaction is injurious to most ferments. Salts of the very heavy metals, and all reagents which coagulate albumen, which obviously prevent their action. Carbolic acid has no constant effect, but salicylic acid checks the action of diastase. The various substances which destroy or inhibit the action of yeasts and other microörganisms, and poisons in general have no constant effect, sometimes hindering, sometimes favoring. If several ferments are present in the same solution, some will act antagonistically to others, but this is not constantly so. Pepsin digests trypsin and ptyalin, but has no action on diastase (Flügge).

Composition of Ferments.—All ferments yet known contain nitrogen, and more or less resemble albuminous substances. Their percentage composition has been, in many instances, established, but no rational formula of their constitution can be given. It is, however, certain that they are very complex, and must possess a very high molecular weight. They can be isolated by various processes, the most important part of which is extraction with water or glycerine, with or without previous precipitation by alcohol or other reagents.

Enumeration of Ferments.—Instances of animal ferments are:

Ptyalin, the ferment of the saliva, which has the property of converting starch into glucose, and is hence called *amylolytic* ferment. The amount convertible is not indefinite; and excess of sugar interferes with the reaction. Found in salivary glands, liver, pancreas, and other parts.

Pepsin.—The active principle of gastric digestion, which converts albumen into peptones. It is found in the mucous membrane of the stomach and in the glands of Brünner.

Pancreatin, or Trypsin, contained in the pancreatin secretion, has the same peptonizing property.

Steapsin; Fat-ferment of the Pancreas.—A substance, not perfectly isolated, which emulsifies fats, and also decomposes them into fatty acids and glycerine.

Amylopsin, a diastatic ferment of the pancreas, converting starch into glucose; identical, at least in its action, with ptyalin.

Inverting ferments, which convert cane and milk sugar (crystalline sugars) into sugars of the glucose class, are contained in various parts of the digestive tract.

Fibrin-forming ferment contained in, or derived from, the leucocytes, which, according to Schmidt, determines the formation of fibrin in coagulation. A **coagulative** ferment has lately been isolated by Woolbridge, which has the property of coagulating blood almost instantaneously.

Rennet.—This well-known substance, obtained from the stomachs of calves, contains a ferment called *Lab-ferment* by the Germans, which has the property of "curdling" milk by coagulating its casein. It is contained in the gastric juice, especially of young animals.

Vegetable Ferments.—An immense number of ferments are formed by plants. We need only mention here—

Diastase of germinating barley, which converts the starch of the grain into glucose in the process of malting. It is also found in numerous other plants. Evidently similar in its action to ptyalin, etc.

Emulsin contained in the bitter almond, which splits up amygdalin into dextrose, bitter almond oil, and hydrocyanic acid.

Peptonizing ferments are contained in some plants. The most definite is papain or papayotin, contained in the Carica papaya, which resembles the similar pancreatic ferment in peptonizing albumens in alkaline solution. Similar ferments are produced by the carnivorous plants, such as drosera, etc.

Inverting Ferments, which convert cane sugar and and lactose into sugars of the glucose class, are produced by certain fungi (penicillium, aspergillus, etc.), but have not been found in the higher plants. A ferment is also obtained from certain plants which has the power of coagulating casein, like rennet.

It thus appears that plants and animals alike can produce the most important classes of ferments, viz., peptonizing, diastatic or amylolytic, inverting and coagulating.

The lower plants such as yeasts, moulds, and bacteria, doubtless produce many ferments, some resembling in their action those produced by the higher plants and by animals, some having peculiar action; but, in most cases, it is not possible to isolate the ferments from the organisms producing them. Hence we cannot speak of them apart from the organisms.

From the above-mentioned facts, a very important pathological law may be deduced, namely, that plants are capable of producing bodies which, even in very small quantities, have the property of setting up most various and potent decompositions in animal tissues. Further, these decompositions are, in some instances, produced in living as well as in dead tissues.

Ferments as Poisons.—It would almost follow from the above law that the introduction of a ferment produced by an organism into another organism must be in some cases injurious; and doubtless this is so, and hence some ferments act as poisons.

But it is not always so. Physiological ferments derived from one animal may exert their natural action on another animal, and thus assist the physiological processes of the latter, as when pepsin from the calf is introduced into the human stomach. Many ferments are quite inert if introduced into a foreign organism. But there are some bodies of this class, which, if introduced into another organism, produce distinctly injurious or poisonous effects.

Moreover, ferments which are beneficial in the alimentary canal by acting on food substances, are poisonous when introduced into the blood and then made to act on living tissues.

Their poisonous effect is chiefly that of tissue-poisons, softening, dissolving or actually destroying, the tissues. In some cases this process makes the tissues more amenable to the action of another class of poisons, namely, microörganisms.

Some ferments also act in some degree as functional poisons, but probably in consequence of a directly injurious effect upon the tissues.

It should be remembered that even peptones, the bodies produced by the action of digestive ferments on albumens, are poisonous when injected into the blood of dogs. They lower the arterial pressure, and may finally produce convulsions and death, and prevent the coagulation of the blood.

ANIMAL POISONS.

Certain noxious substances produced by some species of animals, usually for the purpose of offence or defence, are spoken of as animal poisons, and there are similar substances of vegetable origin which have no general name. Their mode of action is different from that of chemical poisons, being more complex, and different also from the virus of a specific disease, such as anthrax or hydrophobia. Their action is, however, much like that of ferments, and hence this seems the best place to consider them.

The best known of such substances are those contained in the poisonous secretions of certain animals and plants. Snakes, scorpions, wasps, bees, and other poisonous insects, such as caterpillars, sea-nettles or acalephæ, and other lowly marine organisms, also certain fishes (*e. g.*, the sting-ray) secrete substances which have local or general poisonous effects. And these effects are not merely dependent on a chemical irritant such as an acid, though this may account for part of the effect produced, but have at least a strong analogy to the action of ferments.

The poisons of stinging plants, such as nettles, appear to be analogous in their constitution and action. The theory of the genesis of such poisons must be that the organs producing them have been gradually evolved by natural selection or adaptation, in response to the needs of the organism, serving it either in the way of obtaining food or in self-defence.

It does not follow that the fact of these substances being injurious or poisonous to man, is a necessary factor in their evolution. This may be, so to speak, accidental. But the poisonous property appears to be always in some way useful to the poisonous species.

It should be noted that, in the best known cases, the substances in question are not poisonous to the individual or even the species producing them.

It is from this point of view that we can best explain the action of what are called *animal poisons* and some vegetable products resembling them.

Animal and Vegetable Poisonous Ferments.—The poisons derived from animals and producing morbid conditions in man are various in their nature.

The most important distinction is between those which produce poisoning, and those which produce a specific disease.

To the former class belong those conveyed by the bites of venomous snakes, certain insects, etc.; to the latter the diseases of hydrophobia, glanders, anthrax, etc., which will be considered subsequently.

Snake-bite.—A poison secreted by a special gland is injected by a wound produced by the snake's tooth into the subcutaneous tissue, or directly into a bloodvessel.

The local effect of the poison is to produce inflammation, with rapid swelling and often ecchymosis, which spreads for a certain distance from the wound. There is often partial paralysis of the part. The poison of the cobra causes inflammation if applied to the conjunctiva. But it is notable that, if life be prolonged, the inflammation proper subsides, the part becomes cool, livid in appearance, and often passes into gangrene or sloughing.

These facts show that the poison is an irritant and also has necrotic properties, destroying the vitality of the tissues. It is probably related to ptyalin or trypsin, though enormously more potent, just as the gland secreting it is the representative of the salivary glands of other animals, and must be regarded as having been produced by evolution from a simple secretion of the same kind.

Effects of Absorption.—The poison will be most rapidly absorbed from the wound if a bloodvessel be penetrated; but is absorbed also from serous or mucous membranes, such as the conjunctiva, the stomach, and peritoneum, and by the respiratory membrane if applied there.

Passing into the blood it affects nerve-centres, and sometimes the peripheral nerves. The respiratory centre is often affected, and death may be thus caused. The contractility of the muscular fibres may also be affected if the poison be brought in direct contact with them experimentally, or sometimes also through the blood.

The poison also acts septically, producing at a later period sloughing and hemorrhage (Fayrer).

The blood is found fluid after death from viper-poison; but the effect on the blood of cobra-poison is variable.

These results show that snake-poison has the properties both of a *structural* and a *functional* poison.

The active principle appears to be an albuminous substance which has been called echidnine, vipirine, or crotaline. It has most resemblance to a catalytic ferment, which acts in almost inconceivably small quantities.

The blood of poisoned animals is poisonous in proportion to the amount of poison contained in it. There is no evidence that the poison is multiplied or increased in the body.

Insect poisons.—The poisonous principles conveyed by the stings of wasps, hornets, bees, etc., with which must be classed those of other poisonous articulata such as scorpions and spiders, resemble snake-poison in producing inflammatory local effects. They may also produce disturbances of the nerve-centres, such as paralysis, etc., comparable to those of snake-poison, but generally much less intense.

The poison extracted from *Cantharis vesicatoria* is an instance of an irritant which produces inflammation in any surface to which it is applied, and has the same effect on the urinary organs, by which it is excreted after absorption, but does not notably affect the nervous system.

Vegetable Poisonous Ferments.—There are a few substances derived from plants which have some resemblance to animal poisons in their mode of action.

One of the most remarkable is that of the jequirity (Abrus precatorius) contained in the well-known scarlet, black-spotted seeds.

An infusion made from these seeds has a remarkable power of exciting inflammation, a few drops causing severe conjunctivitis if applied to the eye. This was first known practically by being used as a means of curing trachoma by producing acute inflammation which supplants and cures the chronic affection. If applied experimentally to the eyes of rabbits it produces not only inflammation of those parts, but also of the subcutaneous tissue of the face, neck, chest, and abdomen, while the pericardium, pleura, lungs and peritoneum are found much inflamed and filled with a large quantity of exudation, and the animals generally die (Klein).

Since such infusions, if exposed to the air, contain large numbers of a bacillus identical with the hay bacillus (B. subtilis) it was thought by Sattler, the first investigator of the subject, that the inflammatory properties were due to these organisms. But this has been conclusively disproved by Klein, Warden, Waddell, and others, who have shown that the poisonous property is contained in infusions prepared in such a way as to contain no organisms, and that, even when the infusions are swarming with bacilli, the poisonous property is completely destroyed by boiling for a minute or less; though such boiling is known not to destroy the vitality of the spores of the bacilli.

The conclusion is, that the poisonous property depends upon some principle in the infusion, the activity of which is destroyed by boiling; in this resembling several other ferments.

Such a principle has been isolated, and has received the name of *Abrin*. It is a soluble albuminous ferment and has been found in other parts of the plant, as well as in the seeds.

These researches are of great importance in pathology, as showing that we have a substance of vegetable origin which produces inflammation not merely in the matter of chemical irritants, by chemical combination, but by setting up a change in the tissues comparable to the changes caused by the so-called physiological ferments; that is to say, a very small quantity of the substance produces a relatively very large amount of change. By this process the tissues are prepared for the action of the organisms which produce suppuration, viz., certain micrococci; and the resulting inflammation must be regarded as the combined effect of the ferment and the micrococci.

Papain, a vegetable peptonizing ferment referred to above, when injected into the blood favors the development of micrococci. In larger quantity it paralyzes the heart.

Whether the poisons of nettles and such-like stinging plants are of the same kind is uncertain, but probably they are different.

The important thing to note is that the poisonous vegetable ferments are *tissue-poisons*, producing necrosis or disintegration of the tissue-elements, and are thus comparable in their effects to powerful chemical poisons and to physical agents. Thus we can understand how it is that the lower plants, fungi, and bacteria can generate substances which are not only functional poisons, but cause tissue-changes such as those mentioned above.

CHAPTER XXXII.

SEPTIC AND CADAVERIC POISONING.

It is well known that dead and putrefying animal matters are injurious, and even poisonous, to the living; but it has only lately been found possible to isolate and determine the chemical character of any of the substances which produce these effects.

The most convenient method will, therefore, be—first to speak of the general effects produced by putrid matters, and then to mention those constituents of them, actually known, to which these results are attributable.

Cadaveric Poisoning.—Dead bodies, either of men or animals, often contain some poison, or poisons, extremely deleterious, and in some cases fatal, to living persons. This pernicious effect has no relation to the disease which may have been the cause of death, and must be due either (1) to some substance produced in the process of putrefaction, or (2) to some organisms contained in the dead tissues and concerned in the process of putrefaction.

Speaking broadly, the first will give rise to *cadaveric poisoning*, the second to some disease which may be called *pyæmia* or *septicæmia*.

There are, however, abundant facts to show that the first explanation is the only possible one in certain cases. The consideration of the second class of cases will be deferred for the present.

Sudden and fatal poisoning sometimes occurs in persons inhaling the air of tombs or charnel-houses, or the volatile substances given off when coffins are suddenly opened. Terribly sudden deaths from this cause are occasionally reported, and, though rare, these cases have great pathological importance. Such events have doubtless given rise to the stories in old times of plague, or similar diseases, starting from the opening of some long-closed sepulchre. But the symptoms are distinctly those of poisoning, not of an infective disease. They are again quite distinct from the symptoms of poisoning by carbonic acid, sulphuretted hydrogen, or any similar inorganic gas.

It is very likely that some of the well-established cases of sudden or very rapid death by breathing in emanations from plague or typhus patients in crowded foci of disease have been really cases of direct poisoning, and not of death from the infective disease.[1]

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[1] The well-known story, related by an eye-witness (Boccaccio), who saw pigs sniffing at the rags of a man who had died of a plague in the streets of Florence during the great epidemic of 1348, when the animals fell down in convulsions and soon died, is probably to be thus explained. A remarkable instance of fatal cadaveric poisoning occurred at North Uist in 1884. The coffin of a person dead several days was being opened for post-mortem examination, when it burst from the pressure of gases inside

In a more dilute form the same poison or poisons give rise to the well-known injurious effects of the emanations from graveyards in cities and vaults under churches. In the report on Metropolitan Graveyards published in 1850, evidence was given of serious, and even fatal, affections thus originated. Dr. Waller Lewis examined the air of vaults and coffins in numerous cases, and found it to consist of "nitrogen and carbonic acid gases, holding putrescent animal matter in suspension." Ammonia was sometimes found, but sulphuretted hydrogen, or other compound gases containing hydrogen, never. The symptoms produced were faintness, syncope, vomiting, sometimes coma; often followed by diarrhœa and extreme prostration. Since the symptoms produced were clearly not those of carbonic acid poisoning alone, they must be attributed to some animal poison proceeding from the dead bodies.

Fecal Poisoning.—It is a well-established fact that gaseous emanations from decomposing fecal matters, *e. g.* sewer gas, give rise to a distinct form of poisoning, different from any specific disease which may be conveyed by the same channel. It is also well established that recent fecal matters do not produce the same symptoms.

In these cases the effects may be partly due to sulphuretted hydrogen, ammonium sulphide, or other chemical poisons given off in putrefaction, but cannot be wholly thus explained; and we must suppose that, as in the case of cadaveric poisoning, a volatile animal poison is often present in sewer gases.[1]

It is unnecessary to give more instances of illness resulting from this cause, but a word must be said about the relation of these facts to the transmission of specific infective poisons by sewer gas.

There can be no doubt that some such diseases, *e. g.*, typhoid fever, diphtheria, etc., are at least favored by the presence in inspired air of these products of decomposition. Whether the actual poisons producing these diseases are present in sewer emanations is another question which will be spoken of hereafter.

Decomposition-products in the Living Body.—When a part of the living body is undergoing decomposition, like that of dead bodies, poisons similar to, though probably not identical with, those generated in dead bodies, are produced; and being, obviously, placed in conditions very favorable for absorption, may pass into the body and give rise to symptoms of poisoning. This is seen in ordinary gangrene, such as that of a limb. The animal organism is, indeed, so con-

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One of the doctors present fainted, was unconscious for some time, and ultimately died; another was seriously ill (Brit. Med. Journal, April 12, 1884). In 1841 two men were killed in Aldgate churchyard by noxious effluvia from a grave. Similar accidents have occurred in the removal of dead bodies from cemeteries in Paris.

[1] The following is an instance. Twenty-two boys in a school near London were seized in the course of three or four hours with alarming symptoms of irritation in the stomach and bowels, spasms of the muscles of the arms, and excessive prostration of strength. Two of them died in about twenty-four hours. It was found that two days before the attack the contents of a foul cesspool had been spread over the ground near the school (Taylor's Medical Jurisprudence, ii. 124).

structed that, as already shown, inflammation is set up, which forms a barrier to prevent the absorption of the poison from the gangrenous part. But if this be insufficient, symptoms of poisoning, possibly fatal, occur.

The conditions are more dangerous in the case of an irregular wound communicating with the air, when the tissues slough, as it is said. Here, through the absence of a distinct line of demarcation between the dead and the living parts, absorption is more easy and the danger of poisoning greater.

There is a still greater chance of absorption if the necrotic part be quite internal, as in the case of a gangrenous portion of intestine or lung. But even in such a case the dead part may be thrown off and poisoning prevented.

Instances of these conditions are found chiefly in surgical practice, such as traumatic or hospital gangrene, urinary infiltration, strangulated hernia, etc.; but the effects are the same when necrosis is caused by a general disease, such as typhoid fever, measles, etc., or by arterial obstruction.

The symptoms in all these cases are not the same, but have certain features in common, *e. g.*, depression, failure of the heart, collapse; often diarrhœa and vomiting; which are frequently, but not constantly, accompanied by fever and rigors. This group of symptoms is sometimes called septicæmia, septic poisoning, or putrid infection. The first-mentioned name has become ambiguous, being used on the Continent generally for certain specific infectious diseases; and the term infection carries with it a similar ambiguity, hence it is better to say simply septic poisoning. This is rather a condition of the body than a disease. Clinically it is rarely seen in an uncomplicated form, being generally complicated either with the disease which has led to it, or with some special infective disease or diseases, such as pyæmia or septicæmia in the limited sense. That, however, it is caused by tissues in a putrid state is shown by the following considerations among others:

Septic matters, introduced experimentally into animals, produce conditions, often fatal, which resemble, in many respects, septic poisoning in man.

The conditions which favor or hinder septic poisoning supply strong arguments in the same direction.

Septic poisoning is *favored* by:

1. An unhealthy state of the body generally, which predisposes to decay.
2. Retention of the putrid products, as in a wound imperfectly drained.
3. Entrance of matters from outside which set up putrefactive processes.
4. Any conditions which favor absorption.

It is *hindered* by:

1. A vigorous, healthy state of the body.
2. Removal of putrid products, as by the cutting out of sloughy

tissues, or free *drainage*, which is so notable a feature of modern surgery.

3. Preventing the entrance of matters which set up putrefaction, as by very scrupulous cleanliness and by *antiseptic* methods of surgery, which represent cleanliness carried to the precision of a chemical experiment.

4. Conditions which hinder absorption, such as limiting inflammation of gangrene, and healthy granulations in a wound.

It is also important to observe that septic products, like those of cadaveric and fecal putrefaction, appear to favor the occurrence of certain specific diseases. The effect of septic matters in favoring, and antiseptic methods in preventing, the diseases of the puerperal state is a conspicuous instance of this.

The three conditions now described—viz., cadaveric, fecal, and septic poisoning—have evidently many features in common, though the symptoms vary, according to the kind of poison, and according to the dose.

The points of agreement are:

1. The similarity of cause.
2. The similarity of the poisonous substances in so far as they are known in the respective cases.

Causes of Cadaveric, Fecal, and Septic Decomposition generally.—Putrefaction of animal substances is always associated with the presence of microörganisms, viz., bacteria; and the chemical changes which constitute the process result from the vital activity of these organisms.

This law has been established by a long series of researches, and is confirmed by the thousandfold experience of daily life in preserving articles of food.

Putrefaction of these substances is, in our experience, only prevented either by preventing the access of bacteria or by destroying them when present by heat or chemical means, or by conditions which prevent their growth, of which the chief are extreme cold or extreme dryness.

The same is true of dead portions of the human body. But it cannot be too strongly insisted upon that we are now speaking of disease. Disease is a condition of the living body; but putrefaction cannot occur in the living body as a whole, nor in any part of it, unless that part be already virtually dead.

The bacteria which produce these changes may be recognized partly by their form, partly by their effects.

It is not these which constitute the poison in the conditions here considered. The poison or poisons are the chemical products resulting from decomposition.

Numerous experiments have been made on the properties of these substances, taken collectively under the name of septic matters; but only recently have certain substances been isolated which are found to possess in a high degree the poisonous properties recognized as belonging to septic matters generally.

Chemical Products of Decomposition.—In the putrefactive decomposition of animal matters, a vast number of chemical substances are produced. Those which have been distinguished and isolated may be broadly arranged in two groups.

1. Volatile products.
2. Isolable fixed products.

Volatile Products of Decomposition.—These are, for the most part, distinguished by a fetid odor; and this property must not be regarded as altogether accidental in relation to the life of man. It is a warning to us that putrid matters are pernicious; or, conversely, it may be said that the property of the human organism which causes us to regard these matters with horror and disgust, is an instinct of self-preservation, produced by evolution, like other defensive instincts, before any rational account could be given of it, and has been an important factor in the continuance of the human race.

Most species of animals, except those which undertake the task of scavengers, possess similar instincts.

The putrefactive decomposition or fermentation is primarily a splitting up of albuminates, which are first converted into peptones. Gelatine, and substances convertible into it, are also split up, and also the nitrogenous bodies, such as leucin, tyrosin, indol, which are the products of decomposition of proteids.

Albuminates appear to split up into nitrogenous bodies of the fatty and aromatic series, sulpho-acids, etc. These, again, are split up into simpler compounds of the same series, with nitrogen, CO_2, and hydrogen.

These decompositions, which tend to gradually increasing simplification, may take place successively or simultaneously, and hence many stages of decomposition may be present at once in a putrefying substance. Thus the number of chemical bodies produced is very large, and the processes are so complicated that only a few can be represented in the form of a definite equation, and even these do not necessarily express the *final* result.

Among the known products of putrefaction of albuminous substances are:

Hydrogen, nitrogen, CO_2, H_2S, PH_3, CH_4, formic, acetic, butyric, valerianic, palmitic acids; acrylic and crotonic acids; glycolic, lactic, and valero-lactic acids; oxalic and succinic acids; leucin, glycocoll, glutamic acid, aspartic acid (the two latter with leucin are formed also by boiling proteid substances with dilute sulphuric acid); ammonia, ammonium carbonate, and ammonium sulphide.

We find, further, numerous amine bases, as propylamine, trimethylamine, etc. The latter has a strong fishy smell; it is found in herring-brine, and in many plants and animal tissues, especially as the result of decomposition. Another group contains indol, skatol, and skatol-carbonic acid, bodies of offensive odor contained in feces, and obtainable from proteids by action of alkalies. Another important product is tyrosine, with many derivatives thereof, chiefly bodies of [illegible] aromatic series. Tyrosine is obtained from most proteid substances by boiling with sulphuric acid, and also by the action of the pancreatic ferment. Finally, a number of fixed alkaloidal bases called ptomaïnes are constantly produced.

It will be seen that most of the above-mentioned substances can be produced, directly, or indirectly, by the chemical decomposition of proteids in the laboratory. Some of them account for the fetor of putrefactive products, and others partly for the poisonous effects of the gaseous emanations. The most distinctly poisonous are, however, the ptomaïnes, which must be further considered.

Ptomaines or Cadaveric Alkaloids.—These are alkaloidal bases, closely resembling, and in one or two instances identical with, vegetable alkaloids. Attention was first drawn to their occurrence in putrefying bodies as likely to lead to fallacies in the detection of vegetable poisons in post-mortem chemical analysis, but they have now a much greater importance; first as the result of the action of bacteria on proteids; and then because many of them have poisonous properties, which resemble those of vegetable neurotic poisons, and thus explain many of the symptoms produced in septic poisoning.[1]

The most complete investigations have been made by Brieger, who has isolated a number of alkaloids from decomposing fibrin, meat, fish, cheese, gelatine, yeast, and putrid corpses. Others have been obtained from the matters in which bacteria were artificially cultivated.

Among the non-poisonous or slightly poisonous are:

Neuridine ($C_5H_{14}N_2$), a diamine decomposing into dimethylamine and trimethylamine. It is widely distributed, found in putrid meats, cheese, and gelatine, and in the dead human body after the third day.

Cadaverine ($C_5H_{16}N_2$) has an odor resembling that of coniine. It is found in the dead body after the fourth day, but especially from the tenth to the twelfth.

Saprine, isomeric with this, and *putrescin* ($C_4H_{12}N_2$) are found under the same circumstances.

Choline ($C_5H_{15}NO_2$), a compound ammonia base having three atoms, H, replaced by methyl (CH_3) and one by oxethyl (C_2H_5O), which is one of the constituents of lecithin, is found in the first few days of putrefaction, probably arising from decomposition of lecithin, and is then itself decomposed, yielding tri- and dimethylamine, and triethylamine. This base has in a feeble degree the poisonous action of neurin and muscarin.

Among the poisonous bases which Brieger has proposed to call by the general name of *toxines*, are:

Neurine ($C_{15}H_{13}NO$), obtained from meat after five or six days putrefaction, contains H_2O less than choline, and is presumably derived from that, or from its compound lecithin, by dehydration—a process often the result of fermentation and known to be caused by bacteria. Choline may also be easily decomposed, with formation of neurine, in the chemical processes for preparing the alkaloids.

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[1] It had long been known that poisonous substances, probably alkaloidal, were contained in putrid matters, and a body named *sepsin* was isolated by Bergmann and Schmiedeberg, and found to be poisonous, but this was probably not a pure substance. Selmi introduced the name ptomaïnes (*πτῶμα* = a corpse) for alkaloids found by him in the dead body. Nencki first isolated and determined the constitution of a base of this class obtained from putrid gelatine. It is isomeric with collidine = $C_8H_{11}N$. Guareschi and Mosso obtained from putrid fibrine an alkaloid having the composition $C_9H_{15}N$, analogous in its properties to curare.

It is poisonous to frogs and mammalia in very small doses. The symptoms are salivation, dyspnœa, acceleration, followed by depression of the heart, also violent peristaltic action of the bowels, and diarrhœa, ending with convulsions and collapse.

The general effects are most like those of *muscarine*. The latter alkaloid ($C_5H_{15}NO_3$), long known as contained in the fungus fatal to flies, and in many poisonous fungi, was also obtained by Brieger from putrefying fish. Chemically, it is an oxidation-product of choline, and obtained by the action of nitric acid upon it.

Muscarine is a powerful narcotic poison. It contracts the pupil, lessens perspiration, and stimulates salivation. "It has a powerful action on the heart, paralyzing the cardiac muscle and stimulating the inhibitory ganglia. It is a general emetic, and diminishes the activity of the respiratory centre. Its action is completely neutralized by atropine" (Brunton).

Peptotoxine is the poisonous constituent of many peptones, and is formed, for instance, in the action of digestion of fibrin by artificial gastric juice. It can be partially extracted from peptones by alcohol, but its composition is not accurately known. It is rapidly fatal to frogs and rabbits, producing paralysis and insensibility.

Mydaleine.—This and another poisonous ptomaine were obtained from the dead body after two or three weeks' decomposition, but neither is completely analyzed. Mydaleine is a powerful poison, producing in rabbits elevation of temperature, dilatation of the pupils, injection of the bloodvessels of the ears, profuse salivation and diarrhœa, and, finally, great depression of temperature, ending in death. These results, therefore, qualify the statement made above, that poisons, generally speaking, do not raise the temperature. The other ptomaine mentioned was found to cause profuse diarrhœa in rabbits.

The general result of these remarks is to show that ptomaines are powerful *functional* poisons, especially to the nervous system. They have not the destructive action on tissues characteristic of ferments, nor have they necessarily any irritant action.

The production of these bodies by the action of microörganisms on proteids explains many of the symptoms due to the action of bacteria, which will be afterward spoken of.

In the decomposition of animal bodies, it is found that different alkaloids are formed at different stages; and generally, though not universally, the most poisonous are those which are produced in the later stages of decomposition; though at a very advanced stage of putrefaction the poisonous properties are again lost. These results agree generally with the observed facts of cadaveric poisoning.

Since ptomaïnes are such poisonous bodies, and yet are constantly formed by decomposition of proteids, and must be generally or always present in the intestinal contents, it may be asked, How do we escape poisoning through absorption of them from the alimentary canal? The same question might even be asked about peptones, which we have seen to be poisonous when injected into the blood.

The answer to this question doubtless is that under ordinary circumstances the intestines do not permit absorption of these poisonous substances to any great extent, and that what is absorbed is excreted rapidly by the kidneys. But the larger part is thrown out by the bowels, as is shown by the fact that even healthy feces contain substances poisonous to animals. Bouchard, who discovered this fact, supposes that the alkaloids formed in the intestines in twenty-four hours would be sufficient to produce death, if all were absorbed and excretion stopped. It is supposed by some that the transitory or permanent troubles caused by constipation, such as headache, increased arterial tension, and anæmia, are really due to absorption of ptomaïnes.[1]

However this may be, there is little doubt that ptomaïnes or toxines are the cause of the injurious properties of certain articles of food which have from time to time produced poisoning. Sausages have occasionally been found to produce injurious or fatal effects, with symptoms of alkaloidal poisoning, sometimes resembling the action of atropine, sometimes of muscarine, though the poison has not been isolated.

In poisonous fish, however, an alkaloid has been detected which has properties similar to those of some ptomaines, and the same with certain specimens of cheese which have been found in America to produce poisonous symptoms. The alkaloid obtained from the latter has been called tyrotoxicon. In a case of poisoning of a large number of people by mussels, (an occurrence not unknown before), Brieger discovered the cause to be a poisonous ptomaïne, having the composition $C_6H_{15}NO_2$, which he has called mytilotoxine. The mussels were perfectly fresh, not putrid; and whether the poison was produced by them, or was the product of a putrefactive process in the water and only absorbed by the shell-fish, must remain uncertain. Other cases of food-poisoning may probably be referred to similar causes.

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[1] See Dr. Lauder Brunton, On Disorders of Digestion, p. 290. London, 1886. Human urine also, in various conditions, and even in health, is found to contain toxic substances.

CHAPTER XXXIII.

ON SPECIFIC MORBID POISONS.

BESIDES the poisons already spoken of, there is another class called *specific*, because they are capable of producing each one special disease and that only.

The notion of special or specific diseases grew out of the notion of contagion, and though we now know that the property known by this name is not essential to a specific disease, it exhibits the laws of specific morbid poisons in their most distinct form.

It must have been at all times a matter of observation that, in certain diseases, persons who immediately surround the sick, or live where they have lived, or touch objects which they have touched, are liable to contract the disease.

The transmission of disease, whether immediate or mediate, constitutes contagion; and such diseases in which this occurs, are called *contagious* The word *infection* is sometimes used, or was used, for a supposed less indirect mode of transmission than contagion, but it is not really required. The word *infective*, we should remember, is used in a sense somewhat different to infectious, being said of diseases which infect or affect the whole body, as distinct from those which remain local or affect one part only.

Other diseases may be transmitted by insertion of material derived from a diseased person in the body of another person, and such diseases are called inoculable. Some are inoculable which are not in the ordinary sense contagious (anthrax, vaccinia), and some are contagious which are not inoculable (varicella); though the experiment of inoculation has, for obvious reasons, never been tried in the case of many diseases. These two methods of transmission differ, however, only in degree and in accidental circumstances, and both may be conveniently included under one head. If we cali those diseases which may be transmitted in any way from one person to another, *communicable*, we have a word which covers all the facts; but they may also be called, in a broad sense, contagious. Contagious diseases must necessarily be specific, or at least must depend upon a specific morbid poison.

Most contagious diseases are also infective or general, but an exception occurs in the case where the morbid material can be inoculated at different parts of the body at once, or from one part to another, as is the case with ringworm or certain local suppurations such as impetigo. These diseases may be contagious, and often are so in a high degree; but they are not infective or general. The possibility of local inoculation from point to point is indeed a test to show that a disease has not produced a general infection, for when once a general infective poison is introduced, the whole body is modified in such a way as to be insusceptible to a second introduction of the poison. But these non-infective diseases are none the less specific, since in them, as in all inoculable diseases, we have distinct evidence of the conveyance of some material virus.

It is impossible to avoid the conclusion that, as in inoculation, so in the process of contagion, some material substance is conveyed which actually produces the disease, and this is sometimes called the *contagium*. Although the actual contagium is, in the case of a great many diseases, still unknown, the observed laws of the contagious process permit certain conclusions to be drawn as to the nature of contagion in general.

In the first place the contagium has the property of multiplying itself within the body affected by the assimilation of neutral material, so that if an extremely small quantity of it be introduced into the body, it may afterward be found in great abundance in every part, and in some diseases each single drop of blood (for instance) may contain very much more of the contagium than originally produced the disease. Every part or certain parts of the body affected will then come to have the property, possessed by the original contagium, of reproducing the disease. It is evident that this is something very different from what happens in the case of any mineral or inorganic poison. If a small quantity of arsenic or antimony be introduced into the body, it may indeed become diffused into every part and be recognized in the tissues and fluids, but if the whole quantity could be again collected it would only be equal to that originally introduced. The fluids or secretions may be poisonous, but they are so only in proportion to the dose of the original poison which they may contain.

But if, on the other hand, the contagium or virus of smallpox be inoculated at one point of the skin, an immense number of vesicles will be produced, each of which contains sufficient virus to reproduce the disease in several other persons.

Living Contagium.—Thus the multiplication of the contagium exactly corresponds to growth, as of some living thing.

There is also another point in which the analogy with living things is perceptible. The processes set up by contagia are subject to certain laws, to conform to a certain type. After the introduction of the contagium there is usually a period of inaction, or as it is said, of *incubation*, which period is singularly constant in most diseases, and in all confined within narrow limits. Then begins a series of symptoms which may vary greatly in intensity, but seldom or never vary in the order of sequence. For the most part there are signs of a general affection of the whole body, and the disease reaches its acme, after which it may follow one or two courses. Either, notwithstanding the immense increase of poisonous material, the symptoms subside and the disease comes to an end—*i. e.*, it is an acute disease—or else it passes into a *chronic* state, that is to say, the contagium continues to act upon the body for a long time, or for the rest of life.

In the first case what happens is just what would happen if the contagium were a living thing with a short life; the latter case is the would follow if the contagium were living and able to accommodate itself to existence in the body, so as to go on living there for an indefinite time.

These considerations show the hypothesis that contagium is something living to be consistent with the facts. They would not show that this hypothesis is necessarily true, because some other might also explain the facts. But there are certain other considerations which strengthen the supposition.

The contagia of the diseases now spoken of are *specific*; they breed true; each reproduces its own kind, and not another. Hence these diseases (but not all diseases) can be classified, like objects of natural history, by vital as well as by material characters.

Next, the **distribution in place and time** of specific infective diseases follows the same laws as the distribution of organized beings. It has long been recognized that the distribution of plants and animals is not determined by climate alone, but depends upon certain laws, such as those of descent, migration and natural selection. Just so, while there are some diseases which are produced by cold, heat or other physical conditions, the specific diseases generally are certainly not produced, though they may be favored by such causes. These physical causes often have, as in the case of animals and plants, a negative effect—that is, the disease, like the living organism, cannot live under certain definite conditions, or conversely can only live under certain definite conditions of climate, temperature, and so on. But climate and physical conditions do not produce specific diseases. The origin of these is as obscure as the origin of species; their migrations are explicable by the same laws as those of organized beings, and they often accompany, like domestic animals and plants, the migrations of man.

So, too, as regards relations of time. The appearance of specific diseases in great abundance at certain times—*i. e.*, *epidemics*—corresponds to the production at certain seasons of vast numbers of insects or plants, such as locusts, blights, and so forth, the causes of which may be obscure, but which no one now supposes to be causeless or self-gendered.

These relations of coincidence in time and space are so numerous and striking as naturally to suggest the hypothesis that specific and contagious diseases are connected in some way with living organisms, or even that the latter are the cause of the diseases.

Requirements of a Scientific Hypothesis.—But a mere relation of coincidence is not sufficient to establish a scientific hypothesis. It must be shown not only that the supposed cause is adequate to explain the phenomena, but that no other cause is adequate, and, finally, that the supposed cause actually exists.

Of these three requirements the first may be considered fulfilled, on the grounds which will hereafter be stated; the second—viz., that no other cause than living organisms will account for the phenomena—

requires some consideration. The only other hypothesis which can be regarded as adequate is that all specific diseases are produced by some special *ferment;* a view which has gained much support, and has given rise to the term *zymotic* diseases, sometimes used. In modern scientific language the term "ferment" is used in two senses, as explained above; viz., for the chemical ferments called enzymes and for living plants, such as yeast, which act as ferments. Now of these two classes, the only one which exhibits the phenomena above pointed out is that of living ferments, so that nothing but a living organism fulfils the necessary conditions of being the cause of infective diseases.

To complete the proof, it is only necessary to show that the assumed cause, which fulfils the required conditions, actually exists.

In the case of several such diseases the existence of a living contagium, *i. e.*, a microörganism, has been proved; and it cannot be doubted that this is the cause of the disease. In the case of a good many, the proof is still wanting; and their causation must be regarded as not yet clearly established. It may turn out that, as analogy would lead us to suppose, there is some microörganism as yet undetected; or it may possibly turn out that there is some larger law of disease under which the action of microörganisms is comprised.

Specific Non-contagious Diseases.—In a subsequent chapter will be discussed the conditions necessary to a strict proof that a particular disease is produced by a microörganism. In the meantime another question has to be considered, viz., whether, if all contagious diseases be admitted to be specific, there may not be others, not contagious, which are also due to a specific living virus. In such a case the proof would not be so easy, since we should not have evidence of the virus being transmitted from one person to another. Such is ague, which has the appearance of being produced by a specific poison, though it is not in the ordinary sense contagious.

But recent experiments have proved that it is possible to produce ague in healthy persons by the inoculation of blood from a patient having the disease. Tubercle is another instance, which, having been long attributed to various general causes, was a few years ago shown to be capable of inoculation into animals, and thus proved to be a specific disease. Any disease of which the poison cannot be thus definitely handed about, can be proved to be a specific disease only by analogy, or by indirect argument.

Before considering the special kinds of specific poisons, there are some other general laws which must be considered, and the validity of these does not depend upon any assumption as to the nature of the poison.

Entrance of the Virus.—It may enter the body by various channels. Some diseases are received through the skin, in which case it appears as if some small lesion of the skin were generally necessary, as in syphilis and anthrax. The reception of specific poisons through sound skin is open to question. Diseases not generally thus received may be, as has been said, artificially inoculated. Most specific poisons probably enter by the respiratory channels, and may here either affect the entrance of the air-passages, like diphtheria and scarlatina, or first become apparent when they have reached the blood, as in other specific fevers. Some again, are received by the digestive channels, as are typhoid fever, cholera, and dysentery. If we add that some mucous surfaces may occasionally receive a poison in the same manner as the skin does, irrespective of their function, we shall have exhausted the means by which the morbid poisons gain access to the body in extra-uterine life. The mode of access during intra-uterine life or inheritance, is a special question.

Generalization of the Virus.—In most cases, with certain exceptions to be noted hereafter, the virus, after producing certain changes (or sometimes no changes) at the point where it enters the body, becomes conveyed by the lymphatic or bloodvessels to other parts, and is often distributed through the whole body. Its generalization is sometimes shown by the production of an eruption or multiple lesions of the skin, sometimes by profound changes in the blood, sometimes by general affection of many tissues, and sometimes by functional disturbances, notably of the nervous system. These changes may be due to the direct action of the virus itself, or to substances resulting from the action of the virus on the blood or tissues generally. The phenomena are those of the action of functional poisons, and of (necrotic) tissue-poisons, as formerly distinguished. The former are, as a rule, general, though the virus may show a predilection, like inorganic poisons, for certain parts of the nervous system, as in hydrophobia and tetanus for the spinal cord, in typhus for the brain. The tissue-changes are, as a rule, more local, and some poisons show a special tendency to settle down in particular parts of the body and produce their new foci, as it were, of disease. This is the case with syphilis, tubercle, pyæmia, glanders, etc.

Exit of the Virus.—It is a general law of morbid poisons that, in some way or other, they get outside the body again, and thus pass on to a new field of activity. It is in this way that the continuance of the disease is secured. The only known exception to this law is in the case of miasmatic diseases, to be spoken of presently. In all others there is an elimination of the poison, and usually during life, since communication of disease from the dead body, though often possible, is not, in human diseases, an important factor in contagion. The elimination often takes place from the skin, as in scarlatina and small-pox, where dried scales of epidermis are a means of contagion. In others, too numerous to mention, the poison is passed outward with the breath, and the disease thus conveyed.

In others—as typhoid, cholera, dysentery—the virus is ejected with intestinal discharges, and thus finds its way, mostly by indirect means, into the human body again. In hydrophobia, the saliva is at least one channel by which the poison leaves the body, and it is thus communicated by biting. It is sometimes, as in scarlatina, apparently eliminated through the kidneys; but whether it is thus communicable is not certain. This very important fact of the determination of specific poisons to the surface is looked at too much from the point of view of its bearing on the welfare of the patient, and is often spoken of as a providential arrangement intended to cure the disease. But the phenomena attending elimination are often deleterious to the patient, as in the profuse diarrhœa of cholera, and in other cases their beneficial effect is doubtful, since by the time the poison is being thrown off, it is generally no longer a poison to the patient himself. For instance, to inoculate a smallpox patient in a late stage of disease with matter derived from his own vesicles, would be innocuous. But these phenomena are of serious importance, in a dangerous sense, to other persons, and the only existence to which they can be considered as favorable is the existence of the living contagium.

If it be necessary to regard these processes as providential arrangements, they are rather means, provided in the order of nature, to secure the continued existence of the specific diseases.

If we regard the specific virus as a living thing, we might speak of these arrangements as acquired habits of life, by which the virus is transferred from an exhausted to a new soil, like the mechanism by which seeds are wafted through the air. They have also a remarkable analogy, as will be seen, with the processes by which animal parasites, or their offspring, are conveyed from one host to another.

Immunity and Predisposition.—It is a matter of familiar observation that all persons are not equally liable to take all diseases if exposed to the contagion. Those who are insusceptible to the poison are said to possess an immunity, or are called, by a convenient neologism, *immune:* while, conversely, those who appear peculiarly liable to contract certain diseases are said to have a predisposition to them.

The causes of these idiosyncrasies are still obscure, and the subject can only be briefly touched on here.

First, as regards *predisposition.* There are few specific diseases about which we can say beforehand that a person is predisposed to take them. Generally speaking, such a tendency is better marked in the case of simple non-specific diseases, such as catarrhs, chilblains, rheumatic pains, etc. There is, perhaps, only one disease—tubercle—predisposition to which it is thought to be shown by a particular physical constitution. In other diseases, as notably in tubercle itself, we may, with great probability, say that a person is predisposed to a particular disease on the ground of heredity; that is, because his progenitors or other relations have suffered from the same disease. Even this conclusion is liable to many exceptions and qualifications which we cannot consider here.

It is also thought that some races of mankind have a predisposition to certain diseases, but this mostly refers to races in special climates, especially those foreign to them, as, for instance, that Europeans in the West Indies are liable to yellow fever. Facts of this kind are at present too fragmentary to permit any general conclusions to be drawn.

Immunity is a much more definite fact than predisposition. Certain individuals and certain races are quite insusceptible of some diseases, while others possess the same immunity in a minor degree.

Immunity may be *innate*, or it may be *acquired*.

Innate or congenital immunity is shown in such facts as that the negro race never suffers from yellow fever. Among diseases of animals there are many similar facts of total immunity. Moreover, some persons seem to be insusceptible of certain diseases. This is naturally a fact difficult to establish, but is sometimes observed in the case of vaccinia.

Acquired immunity from any disease is generally the result of having had the same disease before, either in its ordinary or in a modified form. In the majority of specific diseases, one attack protects against another for some years, or even for the whole of life; and there is no such complete immunity as in the condition which immediately follows an attack. The same result may sometimes be attained by subjecting the body to the action of the poison in a modified form, *i. e.*, by vaccination.

The explanation of immunity is not easy. The congenital immunity of races against certain diseases has been thought to be due to natural selection. That is, if the disease have acted upon a race during many generations, it will have gradually weeded out the most susceptible individuals.

Immunity acquired by a previous attack of the disease has been explained in several ways. The hypothesis was suggested by Sir J. Simon, and adopted by Pasteur and others. that susceptibility to any particular disease depends upon the presence in the body of a certain special substance or ingredient of the blood, which the morbid poison, so to speak, feeds upon. In one attack of the disease the store of this material in the body will be exhausted, and consequently the individual will not be susceptible to a second attack. The objections to this view are that there is no proof of the existence of any such substance, though the number of them would, by the theory, have to be very large, since there must be one corresponding to every specific disease. A second theory is that the morbid virus produces in the body some material which impedes or inhibits its own life. This is a well-known law of organic life. Animals, for instance, produce carbonic acid, which is a poison to them; and the yeast-plant in fermentation produces alcohol, which, when it reaches a certain degree of concentration, stops the growth of the fungus. So that, regarding the poison as a living thing, this explanation is not unreasonable; but there is a certain improbability in supposing special substances to be produced which remain in the blood for years. A third hypothesis is that the cells of the special part of the body affected by a specific disease, in their combat with the organized germs or exciters of disease (see p. 91), acquire an increased vital energy, which enables them to overcome the same adversaries if attacked by them a second time. But this seems like merely stating the observed law of immunity in other terms, and applying it to the cell instead of to the individual. On the whole it must be confessed that while the fact of immunity is in many diseases well established the laws of its causation are by no means understood.

Enumeration of Specific Diseases.—Although we do not here include *special* pathology, it will be well to give a list of those which we regard as specific diseases, including those which are specific and infective, those which are in addition contagious, and those which are contagious or communicable without being infective. Without describing the symptoms of these diseases, we shall only briefly consider the origin and destination of the morbid poison in each so far as known—*i. e.*, whence the poison is derived; how it enters the body; how far it is distributed within it; what change it produces in the blood and tissues; how it leaves the body, and how it is maintained in existence and passed on to other individuals.

The phenomena of morbid poisons may be classed under four heads:

1. Initial phenomena—*i. e.*, changes produced by the poison at the point where it enters the body.
2. Phenomena of generalization—*i. e.*, the general changes produced in the blood, the fluids generally, the nervous system.
3. Phenomena of secondary local distribution—*i. e.*, changes produced in the tissues of certain parts other than the point of entrance.
4. Mode of existence of the virus outside the body.

In some the phenomena of entrance are so marked that the disease has been regarded as a purely local affection, or it may only occasionally present phenomena of generalization. In others the entrance of the virus into the body is marked by no special symptoms, and its presence is only shown when the phenomena of generalization appear. In such cases the disease has usually a short period, or is *acute*. These latter phenomena are most marked in the case of what are called the acute specific fevers; but modern research has shown that they also belong to other diseases not formerly recognized as allied to this class, especially tubercle and syphilis.

It is to be noted that the phenomena of generalization need not be due to the virus itself, which may be a living organism, but to something produced by it, such as a ptomaïne (see p. 311); and it may be the latter only which circulates in the blood.

The phenomena of local distribution of the poison in the body, or, in other words, the effects of the poison on tissues, are extremely variable in intensity. In many cases the poison is so generally distributed, that no local, or, at least, no important local disease is observable. In others the poison has so special an affinity for, or effect upon, certain organs or tissues, that the disease is remarkably local, and it may be a disputable point whether it is a simple local disease or a general one. This is true, for instance, of whooping-cough, diphtheria, parotitis. But recent research has tended to show that some which were considered pure local inflammations are really due to a specific poison, *e. g.*, lobar pneumonia, rheumatism, etc. In one disease, leprosy, the local effects of the poison on the tissues are extraordinarily severe, while the constitutional disturbance is, at least for a long time, comparatively slight.

The secondary local changes may be broadly described as being the characteristic of inflammation. That is, in the vascular and connective tissues we see hyperæmia, cellular infiltration, and, if the action be long continued, overgrowth; in the parenchymatous tissues, degeneration, destruction, or necrosis.

Hence the chronic local changes due to morbid poisons produce a certain type of tissue only, that called granulation-tissue, and the products have, when they are anatomically distinct, received the name of granuloma or granulation-tumor, *e. g.*, tubercle, and the products of syphilis and glanders.

It is on the mode of existence of the virus outside the body that the spread and continuance of the disease—viz., the laws of contagion, miasma, and so forth—depend.

On the basis of such distinctions as these we may classify specific diseases, as follows, in six groups.

First Class. **Acute Specific Fevers.**—Initial phenomena usually slight or indefinite, but those of generalization and infectiveness very marked; local effects on the tissues very variable; duration limited and usually typical. Some cutaneous eruption generally present. Origin of the poison always, so far as known, from previous cases of the same disease.

The class includes scarlatina, measles, rötheln (or "German measles"), variola, vaccinia, varicella, typhus, typhoid or enteric fever, relapsing fever, plague, and cholera.

Second Class. **Specific Inflammations.**—Initial phenomena, caused by the entrance of the poison, are variable and indefinite; but the poison, when once introduced, has a marked tendency to attack one portion of the body and set up a disease there which can hardly be distinguished from an ordinary inflammation.

Phenomena of generalization variable in degree, but never quite absent; duration usually short and typical; no definite cutaneous eruption. Many of these diseases are highly variable in intensity and also in contagiosity.

When the part specially affected is on the external or internal surface of the body, it is quite possible that this may really be the part where the poison entered, and here may be the initial lesion. The difficulty of determining this point makes the classification of these diseases uncertain, and hence some pathologists classify them as local diseases, others as general.

This class includes whooping-cough, parotitis or mumps, diphtheria, dysentery, erysipelas, tetanus, hydrophobia (pneumonia?) (acute rheumatism?).

Third Class. **Contagious Suppurations.**—Among the initial phenomena, suppuration is especially conspicuous, and by conveyance of the poison to other parts of the body, the same phenomena are produced there, so that the secondary local effects resemble the primary or initial changes. Since the conveyance of virus usually takes place externally, there is not any generalization in most of these diseases.

But if the virus enter the circulation, and be transferred by the circulatory channels, there is generalization of an intense kind, and by transference of the virus to internal situations favorable to its growth, secondary local changes are set up, usually more severe than the initial lesion, and form new foci of poison.

The local or milder diseases of this class are gonorrhœa (contagious ophthalmia?) soft chancre or chancroid, contagious impetigo.

The generalized disease is pyæmia. Gonorrhœa also sometimes shows some phenomena of generalization, the virus being distributed by internal channels to the eye and joints.

The specific poisons of all these diseases are doubtless nearly allied, all producing suppuration. But on careful observation their effects do not appear to be identical. All are, under certain circumstances, contagious or communicable to other individuals, as well as to other parts of the same individual.

Fourth class. **Infective Granulomata.**—Initial phenomena at the point of entrance nearly always distinct. Phenomena of generalization sometimes unnoticed, but when present, like those of specific fevers. Secondary local effects on the tissues very marked. Duration variable, sometimes quite indefinite. No distinct cutaneous eruption.

This class includes tuberculosis, lupus, syphilis, rhino-scleroma, leprosy, glanders (anthrax or malignant pustule?).

Glanders in its two forms, acute and chronic, forms a link between this group and that of the specific fevers.

Fifth class. **Miasmatic Diseases.**—Distinguished by the peculiarity that this specific poison habitually exists outside the human body, and is only received into it from time to time. It is also not communicable, as a rule, from one individual to another, though possibly under some circumstances there may be direct transmission (yellow fever).

This virus is sometimes short-lived in the human body, producing an acute disease, or, on the other hand, it may exhibit strong vitality and give rise to a lifelong malady.

This class includes ague, remittent fever, and other malarious fevers, also yellow fever and dysentery.

Sixth class. **Mycosis or Vegetable Parasitic Diseases.**—In this class the virus is well known and recognizable, but the disease produced has received less attention. These diseases are communicable from one part to another of the surface, whether skin or mucous membrane. The secondary lesions are like the primary; there is no generalization. A few rare cases of internal disease thus produced are known.

This class includes tinea tonsurans, or ringworm, tinea circinata, favus, pityriasis or tinea versicolor, as diseases of the skin; aphthæ or thrush of mucous membranes, actinomycosis of internal parts.

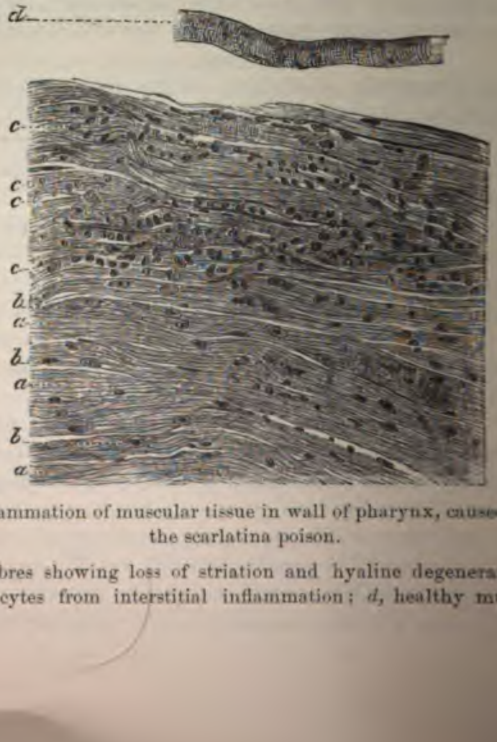
CHAPTER XXXIV.

FIRST CLASS OF SPECIFIC DISEASES ACUTE SPECIFIC FEVE

It is very probable that all diseases of this class are caused living organisms, that is, by some species of bacteria. But since most cases these supposed agents have not been actually proved exist, the consideration of those which are known is deferred for present. The laws now to be stated are valid, whatever theory adopted as the cause of the special kinds of disease.

Scarlatina.—The poison is always derived from a previous case the disease in man, or possibly in some cases from cattle. It ent through the respiratory, or probably sometimes the digestive, muco membrane. It may be, but very rarely is, communicated by inocu tion. After an incubation usually of six to eight days, sometim less, it shows itself in inflammation of the tonsils and adjoining par at once produces fever, and simultaneously, or shortly afterwar affects the skin, producing a characteristic rash. This, along wi

Fig. 73.



Inflammation of muscular tissue in wall of pharynx, caused by the scarlatina poison.

a, muscular fibres showing loss of striation and hyaline degeneration; *b*, mus nuclei; *c*, leucocytes from interstitial inflammation; *d*, healthy muscular fibre comparison.

fever, is evidence of a generalization of the poison. It affects, also, the kidneys, and sometimes one or more joints, and to some extent the intestinal mucous membrane. The disease is acute, lasting one or more weeks.

The poison leaves the body by the skin, by desquamation, being conveyed by the detached epidermic scales, and probably also with the urine. There is no evidence of its passing away with the dejections, but this is not impossible.

During the attack there is immunity from fresh infection, and this immunity lasts for several years, or through the whole of life.

The poison maintains its vitality for weeks, months, or perhaps longer on external objects, such as clothing, which have been in contact with diseased persons. Whether it grows or multiplies in such conditions is not known.

Recent researches of Power and Klein make it probable that one source of the poison is a disease of cows which affects their milk. The poison would then be a distinct species of microörganism, which will be spoken of later.

Morbid Anatomy.—The tonsils are swollen and inflamed, sometimes ulcerated or necrotic, and the neighboring parts more or less inflamed (see Fig. 73).

The ileum sometimes shows signs of inflammation, the Peyer's patches being swollen, hyperæmic, and, in rare cases, ulcerated. The organs most characteristically affected are the kidneys. These show inflammation, which is sometimes not distinguishable from that produced by other causes, but in early stages shows certain characteristic features.

The lymphatic follicles of the tonsils, those of the neighboring parts of the throat, and of the larynx and trachea, have been found by Klein to show marked changes, partly inflammatory, partly degenerative. Inflammatory changes were found also in the lymphatic glands of the neck.

Scarlatinal Nephritis.—In the earliest stage, the organ is enlarged, and injected with bright red dots or patches, which usually show points of hemorrhage. The epithelium is enlarged in a state of "cloudy swelling," so that the tubes are partially obstructed. So far, there is nothing but what is met with in most febrile diseases, and in cases of poisoning. More distinct changes are seen in and around the Malpighian tufts and the afferent arterioles. An infiltration of leucocytes surrounds these structures, showing an early stage of interstitial inflammation, and spreads among the intertubular connective tissue. The Malpighian tufts are usually swollen, hyperæmic, and conspicuous. They show multiplication of the normal nuclei and degeneration of the capillary wall. Collections of leucocytes may also be seen between the Malpighian tuft and Bowman's capsule, and also sometimes fibrinous material, these being occasionally sufficient to compress the tuft. Similar leucocytes are seen sometimes within the cavity of the adjacent tubes. The intima of the afferent arterioles is often swollen, and, according to Klein, there is a proliferation of the nuclei of the muscles, and in some cases the arteriole contains a embolus of granular material.

Now, summing up these changes, we see that they amount to inflammation of the Malpighian tufts and arterioles, affecting the walls and tissues around, which shows the ordinary type of vascular exudative inflammation with abundant leucocytes; while the epithelial structures of the tubes and Bowman's capsule, and the endothelium of the vessels, show parenchymatous inflammation or degeneration.

These changes are just what would occur if an irritant or morbid poison, circulating in the blood, were arrested in the arterio-glomerular apparatus and excreted with the exudation from the Malpighian tuft. These (glomerular and peri-glomerular) inflammations are, in a word, the *track* of the morbid poison as it is being excreted.

If the scarlatinal inflammation lasts for some weeks or becomes chronic, the appearances do not differ from those met with in other forms of diffuse nephritis or Bright's disease, showing both interstitial and parenchymatous inflammation. Dropsy is a frequent result both of the acute and of the chronic kidney affection.

Klein found changes in the arteries of the spleen similar to those described above as occurring in the kidneys; and also changes in the lymphatic follicles like those found in other lymphatic structures. Some arteries in the liver showed similar changes; and there was inflammation of the interlobular connective tissue, constituting acute interstitial hepatitis.

Measles.—The poison of measles is always derived, in our experience, from a previous case of the same disease. It has an incubation of seven to twenty-one days. The first effects are fever and local inflammation, seen in the nose, where it produces catarrh, and spreads to the eyes and air passages, while usually on the fourth day the characteristic rash appears, with increase of fever. This fades about the sixth day, and the fever declines. The chief complications are inflammation of the bronchi and lungs (broncho-pneumonia), sometimes diarrhœa.

There is thus evidence of the poison being widely distributed through the body.

The poison appears to leave the body chiefly, if not entirely, with the breath, and this emission is most marked early in the disease, even on the second day. The contagion is extremely virulent, so that it may be said, there is no protection against it, except a previous attack of the same disease.

The passage of the poison through the body produces a definite change in the blood and tissues, and not unfrequently, in children predisposes to other diseases, such as tuberculosis. Measles supplies a striking instance of the influence of inherited immunity, or partial immunity; so that while in countries where it is common it is usually a mild disease, it is a very serious one in countries or among populations where it is introduced for the first time, and produces a large mortality. It must be supposed that by such an epidemic the su ceptible individuals are weeded out, so that a subsequent infection would find the population less liable to the disease.

Rotheln, Rubella, or German Measles.—The poison is believed to be always derived from a previous case of the same disease. The incubation period is on an average fourteen days, but may vary from six to twenty-one. A skin eruption is produced, which is very often the first sign of the disease. It lasts from two to four days. There is generally slight fever, with an almost entire absence of the catarrhal symptoms of measles. The cervical lymphatics are enlarged. The disease subsides in about a week and leaves no sequelæ. It is distinctly contagious, and the contagiousness lasts for a month or more.

The tissue changes are so slight that nothing can be said about the morbid anatomy of the disease; one attack protects against another with almost absolute certainty; but it affords no protection against the contagion of measles, nor does measles protect from it.

The last named fact is the chief evidence of the distinctness of the disease, but the symptoms are often so slight that, but for the rash, it would hardly be recognizable as a distinct disease.

Smallpox or Variola.—The poison is always derived from a previous case of the disease. It may be inhaled, or may be conveyed by inoculation, the course of the disease differing somewhat in the two cases.

If conveyed by ordinary infection and received with the breath, the disease has an incubation of about thirteen days, when fever, usually sudden and severe, with temperature of 104°, or even 106°, occurs, and is followed in forty-eight hours by the characteristic eruption. But, before this comes out, rashes, resembling those of scarlatina or measles, are sometimes seen, especially in vaccinated subjects. The coming out of the true eruption is accompanied by a marked temporary decline of fever, the temperature often falling some degrees, though still remaining high.

The eruption is at first papular, then vesicular, then pustular and reaches its development in eight or nine days. After this there is another increase of fever, called the secondary fever, concurrently with which the pustules discharge their contents and form scabs. After this the disease usually begins to decline.

Inoculated smallpox differs somewhat from the disease acquired by ordinary infection. The period of latency or incubation is seven or eight days. On the second day after inoculation a small papule shows itself at the seat of puncture, which on the fourth becomes an umbilicated vesicle. On the seventh day this has formed a pustule, and the lymphatic glands are swollen. On the eighth day general symptoms of the invasion of the disease occur. Two days later the inoculated pustule is matured, and the general variolous rash appears. By the fourteenth day the pustule has dried up.

It thus appears that the progress of the inoculated is the same as that of the natural disease, except in the shorter period of incubation, and in being milder generally.

In both forms the poison is widely distributed through the body, being contained in every vesicle, and in the scabs or dried flakes of skin which are shed off from the surface. It is thus multiplied in an extraordinary degree. It also undoubtedly passes into the air, both from the skin and with the breath.

Smallpox is thus a remarkably contagious disease, and the contagium is given off during the whole course of the disease.

Most likely it is communicable from the beginning of the initiatory fever. It may be given by the breath before the eruption has appeared. It continues infectious so long as any dry scabs of the eruption remain adherent to the body; a single breathing of the air where it is, is enough to give the disease. The dead body, for several days after death, has been known to communicate the disease. Clothes, bedding, etc., may retain the infection for a long time, unless thoroughly purified (Marson).

Whether the contagion can be spread through the air, for any notable distance, as from one building to another, is still uncertain, though recent observations of Power make this not improbable.

The body is so far changed by receiving the variolous poison that one attack nearly always protects against subsequent ones.

Morbid Anatomy of Smallpox.—The only important point in the morbid anatomy is the structure of the smallpox vesicle.

The anatomical change in the skin begins with the formation of a round swelling, which appears outwardly as a papule, but is really, as shown by Rindfleisch, in the epidermis itself; the cells of the Malpighian layer swelling up and becoming œdematous. This, with a surrounding circle of hyperæmia, constitutes the red papule of the first stage. The next change is the depression of the centre, forming the "umbilication" of the vesicle, and is due to shrinking of the cells, not to any special connection with the hairs, sweat-glands or other structures. By more copious exudation the outer layer of epidermis is raised up and a vesicle or bladder is formed. But since this exudation is in the substance of the epidermis, not beneath it, the horny layer is not lifted up entire; but a vacuolated or locular structure results, which is very characteristic of the smallpox vesicle. As the exudation increases in the deeper layers of epidermis the whole of this structure becomes separated fron the papillæ. At the same time the cellular infiltration affects the neighboring part of the corium with its papillæ.

In the third stage of the pock the exudation becomes purulent, and the purulent infiltration of the deeper parts causes a considerable destruction of tissue, resulting in a scar. If suppuration does not occur, or is kept within narrow limits, the amount of scarring is very slight.

It should also be stated that the exudation or lymph, both of variola and of vaccinia, contains innumerable spherical bacteria or micrococci, the precise connection of which with the morbid processes will be noticed afterward.

The morbid appearance, of internal organs after death from smallpox are not characteristic. The commonest complication is inflammation of the larynx and trachea. Next to this in frequency is pleurisy.

Vaccinia or Cow-pox.—The poison is derived from cows, and is contained in a vesicular eruption on their udders and teats. It has an incubation of about four days, after which papules appear, which become vesicles, and reach their acme on the tenth or twelfth day. The crusts fall off and the disease comes to an end about the twentieth or twenty-fourth day from the invasion. The general disturbance is slight or unnoticed.

The poison contained in these vesicles is called vaccine-lymph. It may be communicated to man by inoculation, but, so far as is known, not otherwise. When lymph is inserted by puncture into the human skin, a papule is produced about the third day, which becomes a vesicle, reaching its acme on the eighth day. After this some evidence of inflammation (a red areola) is seen around the vesicle, and some fever, with constitutional disturbance, occurs. The vesicle forms a scab on the fourteenth or fifteenth day, which falls off from the twentieth to the twenty-fifth day. In some cases a slight general eruption (erythematous, papular, or vesicular) is produced.

Since the disease may be communicated from one human subject to another, lymph from human vaccinia may be, and generally is, used to convey the poison.

The disease is practically the same if original cow-lymph or if "humanized" lymph is used, except in the former case the local affection is usually more severe, the development is often retarded, and desiccation is slower, so that the crust is often retained till the fourth or fifth week (Marson.)

This disease confers an immunity against itself, which lasts for several years or for life. It also protects to a large extent against smallpox, so that a recently vaccinated individual cannot take that disease; many persons are thus rendered insusceptible for life, and others, if they take the disease, have it in a mild form, so that the proportion of fatal cases in vaccinated is very greatly less than in unvaccinated persons.

The degree of immunity produced is found to be in direct proportion to the severity of the local affection originally produced by vaccination. When the latter operation has been very completely done, the immunity against variola is nearly, if not quite, equal to that conferred by a previous attack of variola. By *re-vaccination* almost complete protection is afforded.

The question whether the poisons of vaccinia and variola are the same is a very important one.

It was shown by Ceely that the variolous contagion might produce in cattle a local disease identical with spontaneous cow-pox, and that the virus thence derived produced the same phenomena in the human subject.

It would appear, then, that variolous virus by passage through the cow acquires the property of producing a mild, almost local, affection instead of a very grave constitutional disease; and that this milder disease produces nearly the same immunity against the more severe form as a previous attack of the latter.

It should be remembered that the disease, as affecting cows, is transferred from one to the other by the intervention of the milkman's hands, and probably through lymph from the cow-pox sores produced on these. Hence the so-called direct cow-lymph has generally, if not always, been passed through the human system. It is, therefore, probable that cow-pox was originally nothing more than smallpox transmitted to domestic cows, and maintained by the relation of cows and their milkers.

Nevertheless this conclusion is not universally admitted. Klein, Chauveau, and others have not confirmed Ceely's results, having entirely failed to produce cow-pox in calves by inoculation of human variolous matter.

A similar affection is known affecting the hocks of horses, which may be transferred to the hands of farriers and thence to other horses, in the same way as cow-pox by the hands of milkers. The principle of vaccination is of great importance in general pathology, having been lately extended to other diseases, notably to anthrax.

Varicella or Chicken-pox.—The poison is always derived, in our experience, from a previous case of the same disease. It is probable, but not certainly known, that the poison is inhaled with the breath.

The incubation is probably about fourteen days (Gee).

On the first day of illness an eruption appears, in the form of red spots, soon becoming vesicles, and lasts four or five days. The accompanying constitutional disturbance is very slight, but there is sometimes considerable subsequent cachexia.

Varicella has never been successfully inoculated. It is probable that the poison is given off from the skin, and with the breath. The disease is quite distinct from smallpox; the infection of one never produces the other, and they confer, mutually, no immunity. It is unaffected by cow-pox vaccination. One attack is, however, absolutely protective against a second.

In rare cases the varicella eruption goes on to form deep ulcerated sores, called Varicella gangrænosa, formerly known as Rupia escharotica. This form is sometimes fatal, but is then nearly, if not quite always, complicated with tuberculosis. The simple form is never fatal.

TYPHUS.

Synonyms: **Petechial Typhus or Spotted Fever.**—The poison is now believed by most pathologists to be always derived by infection from a previous case. It has been thought to be directly generated by dirt, overcrowding, etc., but the recent history of epidemics makes it improbable that these are more than predisposing causes.

The virus outside the body appears to maintain its vitality only among decomposing animal matters and where the air is stagnant (in this respect resembling the common moulds), and is rapidly destroyed by free access of fresh air, or by soaking in water.

When introduced into the human body, it begins to act after a period of incubation of uncertain length and probably variable.

It rapidly becomes generalized, producing, about the fourth or fifth day, a macular eruption which soon becomes petechial, from the escape of blood or blood-pigment.

The virus is remarkable for the profound changes which it induces in the blood more especially, and also in the tissues. The special symptoms, besides fever, viz., nervous derangements and tissue-degenerations, are probably largely due to the poisonous effects of the products of decomposition thus set free. The specific virus is at the same time largely multiplied.

Recent chemical researches on putrefaction suggest that these poisonous substances are probably of the nature of ptomaines (p. 311.)

The immediate effect of these chemical changes appears to be an alteration in the osmotic properties of the blood. By this the interchange of material between the blood and alimentary canal is interfered with. From this arise dryness of the mucous membrane, arrested secretion of saliva and gastric fluid, diminished excretion of chlorine (as chlorides) by the urine, etc.

Another effect of chemical change is altered metamorphosis of tissue, shown by the secretion of an excessive quantity of urea, and qualitatively by the presence of new products in the secretions. There is also a peculiar odor in the skin and mucous membrane, which, in the absence of chemical proof, serves as evidence of some similar change (Buchanan).

Such changes, found to some extent in all febrile diseases, are perhaps more marked in typhus than in any other, except in plague. The duration of the disease is from fourteen to twenty-one days.

The virus leaves the body undoubtedly with the breath, since well-marked instances of infection by inhaling the breath of a typhus patient are recorded; and probably by the skin also.

It becomes diffused in the air around the patient, but apparently less widely than in some other diseases, since rather close proximity or contact is necessary to convey the infection. It becomes attached to clothes, bedding, etc., and may by these be communicated in the absence of the patient. How long it may thus retain its vitality is unknown; but the duration of contagiosity by such means is far less considerable than, for instance, in the case of scarlet fever. A person not suffering from the disease (either because he has had it, or because he is insusceptible) may be the carrier of the disease to others, as has been observed in memorable epidemics of "jail fever."

Immunity is generally given by one attack, but a few authentic instances of second attack are on record.

The nature of the virus is not known, and has been little studied, as of late years, since the introduction of modern methods of research, the disease has been rare.

Morbid Anatomy of Typhus.—The chief changes are in the blood, which is imperfectly coagulated, dark-colored, readily undergoes decomposition, and stains the vessels deeply. The spleen is soft and often large. The lungs generally show deep congestion, especially at the posterior parts and the bases, and are often friable.

The muscles are noticeable by their dark color and softness; the substance is doubtless degenerated, but has not often been minutely examined.

All these changes are evidence of the profound degeneration of the blood and tissues caused by the typhus poison, though there may be little or no special localization of the disease in any one organ.

Typhus has a rather limited geographical distribution. It is not commoner in the British Isles than anywhere else, and especially common in Ireland. Next come those English and Scottish cities which are most frequented by Irish immigrants. But of late years it has been nearly extirpated in England by the "Common Lodging Houses Act," which enforces sanitary precautions and prevents over-crowding in those haunts of the poor. On the Continent of Europe it has not been common during this century, though epidemics have occurred.[1]

TYPHOID FEVER.

Synonym: **Enteric Fever.**—The virus can exist outside the body, especially in decomposing animal matters and polluted water, or in milk. It is generally taken in with water or food; but probably may enter by the respiratory organs also. It has an incubation of, probably, fourteen to twenty-one days.

Fever is produced, which rises regularly for a few days. After a week or more the characteristic eruption appears. There is, besides this, evidence of the general distribution of the virus throughout the body, in the affection of the nervous system, the muscles, and the secreting organs. The disease declines gradually, lasting three weeks or more. There is no doubt that the poison leaves the body by the intestinal discharges, and is thus conveyed into the soil or water, from which it is taken into the bodies of other persons, and in them reproduces the disease. There is no evidence that it is thrown off by the skin or the breath. Hence the disease is very slightly contagious to persons surrounding the patient.

Though it was once thought that the poison might be reproduced *de novo* in decomposing excrement, or even other animal matter unconnected with cases of the disease, recent researches and discoveries strongly confirm the belief that it is strictly specific and always derived directly or indirectly from previous cases. Whether the virus actually grows and multiplies outside the body, or only keeps alive in a condition fit for reinfection in the human body, must be considered as undetermined, but, at all events, one case may give rise to many.

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[1] Even in the last century John Howard, the reformer of prisons, observed that the English "jail-fever" was absent in Continental prisons, though their sanitary condition was as bad as anything in this country. When, however, typhus made its first certain appearance in Europe at the beginning of the sixteenth century, it came from the Mediterranean and spread northward.

It seems that the feces are at first innocuous, or at least do not give off any volatile infecting substance. Whether a full dose of recent typhoid stools taken into the digestive organs would produce the disease is a question not yet resolved (so far as I know) by experiment. But when the feces have undergone decomposition, they certainly contain the typhoid poison, and will reproduce the disease in other persons if taken into the alimentary canal, or, as some think, through the respiratory organs also. The evidence as to this poison being a micro-organism will be given later on.

All evidence shows that the spread of the disease is chiefly, or almost entirely, connected with the arrangements for the removal of excrement, *i. e.*, with sewerage; and with the consequent pollution of water or of milk-supply from this source, or with the emanation of sewer gases.

Morbid Anatomy of Typhoid Fever.—The most characteristic and absolutely constant lesion found in the body after death is an affection of the solitary and agminated glands (Peyer's patches) in the lower part of the ileum, the cæcum, and sometimes the colon. As the disease usually enters the body by the intestinal tract, this is probably the *point of inoculation*.

The earliest change observed is swelling of these glands with surrounding hyperæmia. The Peyer's patches form flattened, oval masses, projecting one-eighth of an inch or more, with the margin still more elevated; the surface being reticulated or sometimes dotted in appearance, or showing merely an irregular mammillated surface. The intercurrent bloodvessels are greatly dilated and injected.

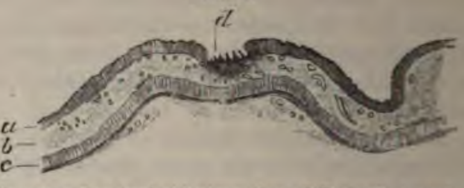
The solitary follicles are less constantly affected. When they are they form shotty projections, from one-eighth of an inch to nearly one-fourth of an inch across.

These changes are always most advanced close to the ileo-cæcal valve and less so the greater the distance from that point.

This swelling depends upon great hyperplasia of the lymphatic elements, whether derived from the blood or by cell-proliferation on the spot. The new elements are mostly somewhat larger than normal lymphatic corpuscles. This lymphatic inflammation constitutes the *first stage*. The cellular infiltration extends beyond the follicles to a certain extent; downward into the submucous tissue; but very little laterally, beyond the Peyer's patch. It attains its maximum after a week (on the ninth or tenth day—Bristowe).

Second Stage.—The lymphatic masses next undergo *necrosis*. The mass becomes yellower and more opaque, and finally the lymphatic follicles, with some surrounding tissue and with the epithelium covering them, break down, either piecemeal, or so as to form one large slough. In the former case, partial or ragged ulceration results (see Fig. 74). In the latter case the epithelium falls off, but the mass of necrotic tissue remains in the form of a slough, stained deep yellow or brown by the intestinal contents, and separated by a clear line of demarcation from the congested surrounding tissue. It is then cast off, perhaps in one piece, perhaps in fragments. The necrotic proces occupies, roughly, another week, so that the separation of the slough takes place in the third week. It is possible there may be a process of simple resolution without ulceration, but this must be rare.

FIG. 74.

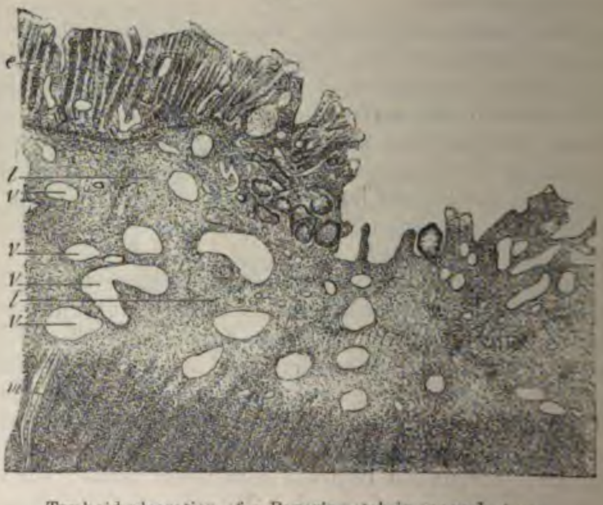


Commencing typhoid ulceration of Peyer's patch.

a, mucous membrane; *b*, submucous; *c*, muscular coat; *d*, commencing ulcer, with lymphatic infiltration beneath it.

Third stage. Ulceration.—The ulcer thus formed appears to the naked eye to have a tolerably smooth floor. The edges often overhang to a certain extent. There is no gradual descent as by steps (often seen in tubercular ulcers). It may involve the whole part of a Peyer's patch; it does not usually extend deeper than the submucous coat; but sometimes the muscular coat may be seen on the floor, and more rarely this is destroyed also, so that the peritoneum alone forms its base. In the solitary glands the lymphatic follicles and a little beyond are involved, and the process is essentially the same.

FIG. 75.



Typhoid ulceration of a Peyer's patch in second stage.

Mucous coat, showing partial disintegration of mucous crypts and deeply stained masses of necrotic tissue; *v*, dilated and engorged bloodvessels; *l*, lymphatic infiltration in submucous tissue; *m*, muscular coat.

Two dangers arise in deep ulcers. Copious hemorrhage from the ulceration of a small artery, or perforation from necrosis of the serous coat. The latter may produce peritonitis and other obvious results, but may be checked by adhesions.

Since the progress above described is limited to the agminated or solitary follicles, the resulting ulcers are oval, with the longer axis in the direction of the bowel and situated remote from the mesenteric attachment, or smaller, round, and scattered.

In rare cases irregular ulceration extends laterally from the Peyer's patches, involving, it may be, a large part of the transverse section of the bowel; but this ulceration is much more superficial, and thus, as well as by the shape, readily distinguished from the normal process. It occurs, in the writer's experience, only in very protracted cases, or when there has been relapse.

Typhoid ulcers heal by granulation and become covered with epithelium, but the lymphatic structures are apparently never restored. The scar is thin, transparent, flexible, and does not lead to contraction of the bowel.

Cicatrization does not begin till after the third week, and occupies an uncertain time, probably several weeks.

The mesenteric glands connected with the affected portion of intestine undergo changes histologically the same as those of the intestinal follicles. In the early stage they are vascular and swollen by lymphatic hypertrophy. In later stages they are pale, yellow, and necrotic. Simple resolution is the ordinary termination of the process, but there may be caseation, or very rarely suppuration.

The process above described has some points of affinity with the production of inflammatory new-growths, such as tubercle, etc. New elements are formed, which are somewhat more permanent than those of acute inflammation, living for days or weeks, but then die and break up, so that they are less permanent than those of the infective granulomata.

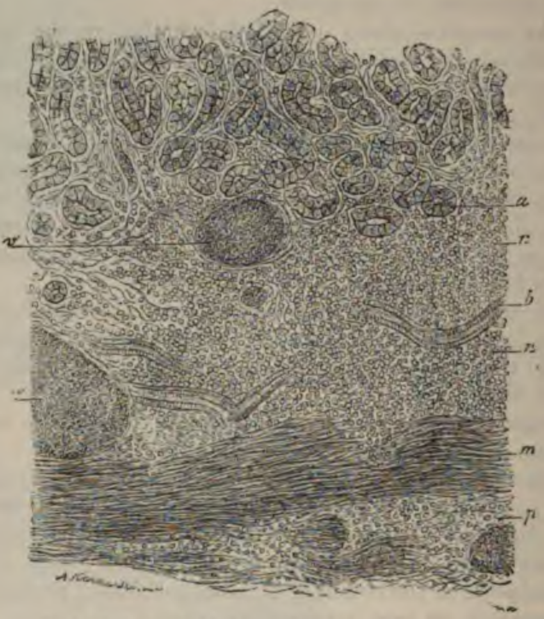
Other Organs Affected.—A very constant change in typhoid is parenchymatous degeneration or cloudy swelling of granular epithelium, seen more or less in most febrile complaints. This is very obvious in the kidneys and in the liver, producing charactertistic changes such as are represented in Fig. 31. Both organs are increased in size.

The spleen is almost constantly enlarged, soft, and dark-colored. It shows general lymphatic hyperplasia, without characteristic features.

Ulceration or necrosis of the larynx sometimes occurs, but its frequency varies much in different epidemics. Inflammation of the mucous membrane of the stomach is common in typhoid, as in other acute febrile diseases (Fig. 76).

Muscle-degeneration in Typhoid; Myositis Typhosa.—This change is seen chiefly in the adductors of the thigh and in the recti abdominis, but also elsewhere. It consists of three processes: (1) Interstitial inflammation; (2) Degeneration of muscular fibres; (3) Regeneration of the same. The first two must be regarded as simultaneous effects of the typhoid poison acting on different tissues, the last as a subsequent process.

Fig. 76.



Gastritis in typhoid fever (Cornil and Ranvier).
a, a, gastric glands; *v, v*, engorged bloodvessels; *b*, arterioles; *n, n*, and *p*, lymphatic infiltration of submucous tissue; *m*, muscular coat.

1. A small-celled infiltration is seen in the interstitial connective-tissue of the muscle, which, whatever may be the origin of the cells, is clearly nothing more than a moderate degree of inflammation. Rindfleisch has pointed out that the cells are somewhat larger than ordinary lymph or pus-corpuscles, and that this process is thus comparable to the lymphatic hyperplasia of the intestines and glands above described.

2. Many muscular fibres, but not all, undergo a peculiar form of degeneration. After passing through a stage of cloudy swelling, the muscle-substance loses its striation, and becomes translucent, hyaline, or, as it is called, *vitreous*. The change is somewhat similar to, but more marked than, that shown in Fig. 73 as the result of the scarlatinal poison. These swollen and vitreous fibres break up into polygonal masses, probably through the contraction of neighboring fibres, which are not affected. Rupture of large bundles sometimes occurs, producing hemorrhage or abscess.

3. The degenerated fibres are slowly absorbed, but in the meantime there are always seen along with them certain other fibres clearly immature or newly formed, showing that a regeneration of muscular tissue is taking place. This new formation takes place, apparently

from the persistent muscle nuclei and within the sarcolemma (but there is some difference of opinion on this point). If so, it is comparable to the regeneration of fibres after other inflammation shown in Fig. 22. But the whole of the destroyed tissue is not always restored, so that a gap, partly filled by fibrous tissue, remains.

The lungs and air-passages are often affected in typhoid. Bronchitis is very common. There is sometimes a hypostatic pneumonia.

The nervous system is widely and injuriously affected by the typhoid poison, as is shown not only by nervous prostration and other symptoms of the disease, but by the serious sequelæ—paralysis, insanity, etc.—which sometimes follow.

Relapsing Fever, Spirillum Fever, much resembles typhus and typhoid, and was formerly confounded with them. The source and habitat of the virus outside the body are unknown. It enters the body either with food or air; with which, is as yet uncertain.

But it has been shown by Carter that it is inoculable, by means of the blood of an affected person, into monkeys, and from these to other monkeys.

The incubation period, when inoculated, is about two to five days. The length of incubation when otherwise acquired is uncertain.

The fever produced is remarkable for its discontinuity, showing several relapses. The blood during the crises contains a specific organism, a *spirochæte.* It is not known to be contained in the secretions, so that the ultimate fate of the virus is unknown.

Decomposition of blood and tissue-changes are much less marked in this fever than in typhus and others.

Bad sanitary conditions, especially starvation, strongly predispose to the disease; hence it has been called Famine Fever.

Plague; Oriental or Bubonic Plague.—The poison of this disease is evidently analogous to that of typhus. It retains its vitality outside of the body in places where there is much decomposing animal matter, and is hence remarkably fostered by uncleanliness, while abundant fresh air and fresh water appear to be the most efficient agents in destroying the poison. It appears to resemble the organisms which produce putrefaction, since the changes which it sets up in the human body have some resemblance to putrefactive changes. It is communicable from one person to another by direct contagion, and also adheres to clothing and other articles, and in a special manner to buildings. In some places it preserves its vitality from year to year in houses, and even sometimes apparently in the soil, so that it is to some extent a miasmatic disease as well as contagious.

It has often been conveyed from one country to another by infected persons, and probably also by infected objects.

As in the case of typhus, a person not suffering from the disease may be the vehicle of contagion. It is thought that the poison may retain its vitality for months or years, but this is uncertain except where, as stated above, it is miasmatic. Infection may be conveyed by a dead body. The general laws of contagiosity of plague closely resemble those of typhus.

The period of incubation is usually a week, but may be less—even, it is thought, less than twenty-four hours. It produces, in the human body, high fever and decomposition of blood and tissues, like those produced in typhus, but more marked. The most striking evidence of these changes is that free sulphuretted hydrogen gas was found in the blood of living patients by French pathologists in Egypt. There is no characteristic eruption, but dark, hemorrhagic patches often come out on the skin in late stages—the so-called "tokens," usually presaging death.

No disease is more influenced in its epidemic occurrence by temperature than plague. In temperate climates the vitality of the poison is usually checked by the cold of winter, though it may be kept alive in houses by artificial warmth. On the other hand an air temperature of 85° at once checks the diffusion, and one of over 110° kills the poison outright.

Morbid Anatomy of Plague.—The general appearances closely resemble those of typhus, with even more marked signs of decomposition. The great difference is that lymphatic inflammations or buboes are almost always found in plague, and are rare or exceptional in typhus.

The geographical distribution of plague is most remarkable, and this alone would show it to be specifically different from, and not merely a variation of, typhus. It is unknown in the tropics, and in temperate climates suited to it has a very limited range. Formerly it occurred frequently in various parts of Europe, and at the beginning of this century was almost constantly present in Turkey, Egypt, and Asia Minor; but it is now entirely extinct in those countries, and is not found in Asia west of the border-land of Persia and Mesopotamia. Certain parts of Northern India and Southern China, with scattered spots in North Africa and Arabia, are the only other known stations.

ASIATIC CHOLERA.

The proof that cholera is a specific disease rests, in the first place, on its history and geography. The disease, as now known, is first recorded in an epidemic form as having occurred in 1817 in Bengal, though the imperfection of Indian records does not permit us to say how long it may have previously existed as a local disease. At all events it first appeared at this date as a spreading disease; shortly afterward it extended throughout India and to Burmah and China, and in 1829–'30 through Russia to the whole of Europe, and thence to America. In the successive recurrences of cholera since that time it has in like manner spread from its original home to other countries which it has colonized, so to speak, for one or several years, rarely more than three; but it has not taken permanent root in Europe, Africa, or America, nor apparently in any part of Asia except India. We regard it, then, as a disease indigenous in Lower Bengal, and specially in the delta of the Ganges, but elsewhere as an exotic. These facts would be almost enough to show that the disease is specific, since climates like those of Bengal in other parts of the world do not produce it, and this conclusion is confirmed by the manner of its extension, which always accompanies and is marked out by the lines of human intercourse. We conclude, therefore, that the poison is carried by man, and probably almost always by people actually suffering from the disease. This law is sometimes obscured by the fact that the poison appears to require some incubation, passing first into the soil and then into other human bodies. It rarely or never passes directly from man to man through the air, though some think that this may happen in ill-ventilated rooms crowded with cholera patients.

When patients convey cholera to a fresh place or country, it is then usually by infecting the soil, and the results of this infection may not be apparent for some time after, or even not till the next year. There is little doubt that the poison is contained in the intestinal discharges, but opinions differ as to whether these are immediately poisonous or only after they have undergone certain changes. As in the case of typhoid fever, direct experiment must be at least rare; still Macnamara states that several people acquired cholera from drinking water into which cholera stools had passed some hours previously, and which was exposed to a hot sun. When it passes into the soil or water it apparently undergoes multiplication, so that one case may supply material for infecting many persons. Moisture appears to be essential to its vitality and growth; but it flourishes especially in soils which are moderately damp and at the same time hot. According to Pettenkofer, the development of the poison is influenced by the amount of the subsoil water, whence a miasma is produced which becomes diffused in the air. The latter point is, however, still one of great difficulty.

Reception of the Poison.—There can be little question that the cholera poison is in most cases received by the digestive organs, and especially, though not solely, through the medium of water. It is not impossible that the poison may be received by the organs of respiration, but this point is not established beyond doubt.

The action of water as a distributor of cholera poison has been established by incontestable proofs in many instances. One of the best marked was that of the London cholera epidemic in 1866, which was practically confined to the district supplied by a certain water company. How the poison got into the water furnished by this company was not absolutely established, though some suspicious evidence was brought out. It is probable that water must be contaminated with organic matters in order to be a proper medium for the growth of cholera poison, but there is no proof that what is considered pure water may not be the means of conveying it. Uncooked vegetables and fruit are also regarded as means of infection.

When bedding or other objects soiled with the excreta of cholera patients convey the infection, as seems to be a well-established fact, it is supposed that the poison must be inhaled with the breath. Whether it can be inoculated into a wound, has never, so far as I know, been determined.

All attempts to convey cholera to animals by inoculation, feeding, or otherwise, have proved unsuccessful.

Symptoms.—It may be enough to say here that the first stage, that of a *collapse*, with profuse evacuations, cramps, algidity, and collapse, resembles certain kinds of poisoning, and has often been compared to arsenical poisoning, though perhaps more like the symptoms produced by muscarin or mushroom poison (see p. 312). It is not accompanied by fever. The second stage, that of reaction or secondary fever, is more like an ordinary febrile disease.

We must suppose that there is a generalization of the virus, or of some of the products of the virus, perhaps alkaloids of the toxine class, which produce the nervous and general symptoms.

Summary.—The specific virus of cholera appears to be endemic in certain countries, to be transferred to others by human beings, to have the power of living and increasing in the soil of water, and probably also of increasing as well as living in the human body. It has, therefore, the properties of a living thing, and the symptoms it produces are like those of poisoning by alkaloids generated by low forms of vegetable life. Hence the presumption that the original cause of the disease is a vegetable organism is a very strong one. Whether this organism has been actually found is a question to be considered hereafter.

Cholera differs from the purely contagious diseases, because the virus, though communicable, has an independent existence in nature outside the human body, that is, it is a miasmatic disease also, at least in those countries where it is endemic.

Morbid Anatomy of Cholera.—The external appearance when death takes place in the stage of collapse is characteristic: the face is shrunken and ghastly; the skin is livid in parts; rigor mortis well marked. Temperature sometimes rises after death. The muscles are dark-colored. The brain shows no characteristic appearance, being in some cases congested, in others showing excess of fluid. The lungs are dry and collapsed, moderately or sometimes excessively full of blood, but in other cases said to be anæmic. The heart usually shows the fulness of the right side and emptiness of the left characteristic of the asphyxial mode of death; but Macnamara asserts that immediately after death both sides are equally full, and that the accumulation on the right side takes place subsequently. The blood is usually thick and dark-colored, as if from loss of water. The most notable appearances are in the intestines. These are, when death occurs in the stage of collapse, small and contracted, containing little gas. The serous surface is pale or mottled with a rosy pink color, different from the usual dark staining of the bowels after death. Dr. Moxon attributes this difference to the absence of the gases of putrefaction. The contents are some tenacious mucus with a variable amount of fluid containing a quantity of desquamated epithelium. This appears to be shed off to a certain extent during life, but chiefly a few hours after death. There are usually no natural feces and no bile in the intestines. When death does take place, however, in the latter stage the bowels are congested, and their contents dark and bile-stained.

The intestinal glands are generally enlarged, Brünner's glands in the duodenum very constantly. The lymphatic masses of the solitary and Peyer's glands in the ileum are also enlarged sometimes, so as to recall an early case of typhoid, and slight ulceration has been observed.

The other organs show no constant changes, but the kidneys are in some cases hyperæmic, and in latter stages may be greatly enlarged and congested.

Owing to the great drain of water from the tissues, the organs are generally well preserved, and decomposition is long delayed.

CHAPTER XXXV.

SECOND CLASS OF SPECIFIC DISEASES. SPECIFIC INFLAMMATIONS.

Whooping-cough. Pertussis.—From the contagious character of this disease, and from its occurrence in epidemics, and its absence for long periods in certain places till reintroduced by a new case, there can be no doubt that it is due to a specific poison.

Where the poison exists outside the human body, or whether it has any real vitality under such circumstances, is unknown. It has an incubation period of about fourteen days.

When introduced it is through the respiratory channels, and it lodges on the mucous membrane of the larynx, trachea, or, perhaps, deeper in the bronchial tubes. There it produces a catarrhal inflammation, which is distinguished from other catarrhs by the excessive degree in which the nerves are irritated, so that spasmodic cough and other well-known symptoms are produced. There is always some fever.

This inflammation at first resembles an ordinary catarrh, and hence it has been thought that ordinary catarrh predisposes to the reception of the poison, or even that this will not take root on a perfectly sound mucous membrane. But probably the immunity which some persons show is due chiefly to having had a previous attack, or to want of constitutional liability, or to accidental circumstances. It is rare for any child in a family or household to escape, if the disease be introduced.

There is no distinct evidence of a generalization of the poison in the body, the other symptoms being due either to reflex nervous action, or to the cachexia induced by the disease.

The poison leaves the body by the respiratory channels, in sputa, and possibly in a volatile form. It is not known to be excreted by any other channel. Masses of sputa, etc., dried on linen, retain the poison in an active state for some considerable time, probably for weeks. There is no evidence of the poison growing or multiplying in such a situation. One attack gives almost absolute immunity against a second. Hence it is rarely seen in adults.

The specific poison of whooping-cough has been identified. Numerous microörganisms are found in the sputa; but it is not known that any of these is the cause of the disease.

The morbid anatomy of whooping-cough shows nothing distinctive except signs of catarrhal inflammation and the morbid changes due to complications, such as broncho-pneumonia.

Parotitis or Mumps.—There can be no doubt that this contagious and sometimes epidemic disorder is due to a specific poison, but little or nothing is known as to its nature. So far as experience goes, there is no cause of mumps except infection from a previous case.

After an incubation of eight to twenty-two days (Ringer) some fever is produced, and simultaneously or shortly after, an inflammation of the parotid gland on one or both sides, sometimes of the submaxillary also.

As the poison is probably taken in, and certainly excreted by the breath, the probability is that it settles on the mucous membrane of the mouth, and attacks the salivary glands thence.

There are no general phenomena except fever and its usual accompaniments, so that in the great majority of cases no evidence is given of any generalization of the poison. But in some cases an inflammation similar to the original is produced in the testicles in one sex, or the mammæ or uterine organs in the other.

This is called *metastasis*, and since the only practically conceivable channel of communication between the organs originally and those secondarily affected is the blood, we must assume that the poison is distributed by the blood. Severe constitutional symptoms sometimes accompany this metastasis.

Some would prefer to call mumps a general disease, and suppose the poison enters the circulation and attacks the salivary glands as a seat of election, owing to some peculiarity of tissue, while the other organs affected possess this susceptibility in a minor degree. This hypothesis can neither be proved nor disproved, but that of a local origin of the disease seems more probable.

It is not known whether the poison of mumps can be conveyed by non-living material objects. One attack appears to confer immunity.

The morbid anatomy of mumps may be said to be unknown, as the disease is so rarely fatal.

DIPHTHERIA.

Definition.—A spreading inflammation, usually of the tonsils, fauces, larynx, and adjacent parts, also occasionally of other mucous surfaces and wounds, caused by a specific poison, the nature of which is not yet accurately known. But the evidence for the existence of such a poison rests upon numberless facts of direct inoculation and contagion.

The virus is received into the mouth or air-passages and there produces the initial inflammation. There is some evidence that a previous state of catarrh strongly predisposes to the reception of the poison. Variable, though often very grave, general symptoms are produced, which appear to depend upon the absorption of a poison from the affected part.

The characteristic false membrane, and mucus from the same parts or saliva, are undoubtedly carriers of the poison and reproduce the disease if conveyed to the mucous membranes or wounds of healthy persons.

The poison retains its vitality for an uncertain length of time on clothes, bedding, the interior of rooms, etc. It does not appear to be easily conveyed through the air, but may be communicated by the breath.

Hence the contagiosity of diphtheria appears to be largely influenced by accidental circumstances, and varies enormously in different cases and in different epidemics. Constitutional predisposition plays a large part in the spread of the disease; some persons enjoying apparently an immunity against the poison, others being remarkably predisposed to be affected by it.

The source of the diphtheria poison and its habitat outside the human body are still involved in great obscurity. It is generally thought that the accumulation of excrement, etc.—in a word, bad sewerage—favors its development, but this cause certainly does not act universally. On the other hand, diphtheria occurs in perfectly healthy places, and is, on the whole, more common and destructive in country districts than in cities. It has sometimes appeared to be conveyed by food, as milk.

Since it is not possible always to trace diphtheria to a previous case of the same disease, it is possible that the poison is a microörganism which lives in soil or water and occasionally gains access to the human body. It is not generally known as a disease of animals; but some species of animals suffer from diseases which are at all events very similar. The diphtheria of pigeons is a well-known disease producing false membranes like those of human diphtheria, and is both contagious and inoculable. A similar disease, but probably not the same, is known to affect fowls, and pseudo-membranous diseases of the air-passages have been observed in cats, horses, and swine. In a good many instances maladies of this kind in animals have been found occurring simultaneously with, or preceding, human diphtheria; but precise proof that the disease in animals has caused the human disease is at present wanting. Such transmission, if established, would, however, explain some of the cases of apparently spontaneous origin of sporadic cases of diphtheria. On the other hand, it is certain that human diphtheria may be communicated to some animals by inoculation.

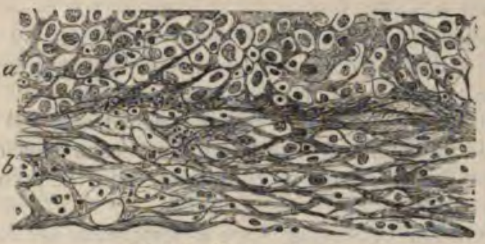
Morbid Anatomy of Diphtheria.—The characteristic lesion of diphtheria is the formation on the affected surface of a layer of material adhering with more or less tenacity to the subjacent tissue, but usually shed off in the form of what is called a false membrane.

This membrane consists of a sort of network of fibres and hyaline material entangling numerous cells, which are partly blood-disks, partly leucocytes, partly more or less altered epithelia of the mucous membrane. The hyaline or amorphous substance itself may also be shown to be made up partly of degenerated cells which have undergone a process described as coagulation. By tearing up the membrane, altered epithelia, smooth, glassy, and varying in form, may be detected.

The subjacent and surrounding tissues are highly congested, and present various degrees of inflammation.

In the most characteristic form, seen especially on the tonsils and fauces, or sometimes on the base of the tongue and in the mouth, this membrane is removed with some difficulty from the subjacent tissue, and after removal exposes a surface generally bleeding, excoriated, or otherwise altered. This surface will generally again give rise to a product similar to that already removed.

FIG. 77.



Diphtheritic membrane.
a, infiltrated tissue; *b*, fibrinous layer, entangling cells.

If the process extends, as it often does, into the air-passages, the appearances produced are somewhat different. The false membrane is much more easily detached, either during life spontaneously, or on post-mortem examination. It often lines the trachea completely, so as to form a hollow cast, and may extend into the bronchi and bronchial tubes, sometimes very far down. Where the false membrane ceases, the surface generally shows ordinary catarrhal inflammation, with abundant muco-purulent discharge.

The false membranes on these surfaces (with columnar epithelium) are somewhat different from those on the fauces. The surface under them is generally apparently unaltered, or simply inflamed, not excoriated or bleeding. The membrane itself is made up of cells and fibrinous network in varying proportions. The network is often delicate and purely fibrinous in appearance, sometimes thicker and apparently made partly of fused epithelial cells. The cells are partly leucocytes (with few blood-disks), partly epithelia, which are often very little altered, so that in the latter case it may appear like a mere exfoliation or desquamation of the epithelium, glued together by a certain amount of fibrinous exudation. (Hence the great diversity in the description given of these membranes.)

It is, therefore, difficult to distinguish between the membrane itself and the tissue; so that the former must be regarded as dead or necrotic tissue.

It will be seen in the figure that the superficial portion (*b*) consists of a network, the trabeculæ of which are much thicker than a regular coagulation of fibrin, while the deeper portion (*a*) consists essentially of tissue, permeated by more irregular masses of the same kind, while the cell-forms are better preserved. Very great variations are, however, met with as regards the proportion of cells and of intercellular substance. There is, undoubtedly, some albuminous exudation, but this is chiefly *interstitial.*

In some cases the process is limited to the epithelial layer (diphtheritis superficialis), in others it extends more deeply into the sub-epithelial connective tissue (diphtheritis profunda). There is often suppuration, and a distinct ulcer is sometimes produced and remains.

The above-described process is the classical diphtheritic inflammation, sometimes seen also on other parts, as on the genital mucous surfaces and on wounds.

The process is limited, almost without exception, by the basement membrane on which the columnar epithelium rests, though the subjacent tissue may show some ordinary inflammation.

A membrane such as has just been described is called croupous. It resembles the inflammatory exudation on serous surfaces (allowance being made for the difference in the tissue), and the exudation in the air-cells in pneumonia.

An inflammation producing such a membrane on the trachea and air-passages is usually called croup, and much controversy has arisen on the relations of croup and diphtheria, which cannot be fully discussed here.

It should, however, be stated—

1. That a croupous membrane is readily produced in the air-passages of animals by irritating substances (ammonia, acetic acid, etc.), and is, though rarely, produced in man by simple irritation, such as by boiling water or steam, or even by other irritants, possibly by cold.[1]

2. A process resulting in the production of similar membrane, *i.e.*, anatomically croup, is, however, often set up by the poison of diphtheria.

Hence the *disease* diphtheria may give rise to a croupous inflammation of the trachea simultaneously with a necrotic (so-called diphtheritic) inflammation of the fauces, and the difference between the croupous and diphtheritic membrane depends upon the anatomical structure of the part on which each respectively is formed.

Membranes formed on the larynx vary in structure as the epithelium of its parts resembles the faucial or the tracheal epithelium.

Microörganisms in Diphtheria.—Microörganisms are frequently met with in the diphtheritic membrane. Masses of micrococci are most commonly seen, both on the surface and in deeper parts. Certain forms of bacilli have also been described. Little importance can be attached to the first of these in relation to the causation of the disease, because in the dead tissues exposed to the air such organisms find an appropriate soil. A large number of micrococci and bacilli are also found normally in the mouth, and would readily make their way into the diphtheritic products. Later researches, in which it has been attempted to discriminate forms which may be really pathogenic, will be referred to hereafter.

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[1] See Report of Committee on Relations of Membranous Croup and Diphtheria. Medico-Chirurgical Transactions, vol. lxii., 1879.

Many attempts have been made to communicate the disease to animals by direct inoculation, or by introducing diphtheritic products into the throat or air-passages. The results are conflicting, but in some of Oertel's experiments on rabbits, introduction of fragments of membrane into the air-passages produced a membranous inflammation of those parts, followed by general symptoms of infection and disease of the kidneys, with death in two or three days. Inoculation of similar material into wounds of muscles and into the cornea, has also produced, in the experience of several experimenters, a spreading inflammation and rapidly fatal general disease, but without distinct symptoms of diphtheria.

Other Organs Affected. Lymphatic Glands.—The throat affection spreads, in the first place, to the dependent lymphatic glands. These become swollen and inflamed as in other spreading local inflammations. In diphtheria the fibrous tissue surrounding the glands, as well as the subcutaneous connective-tissue, are very notably affected, producing a general œdema, and sometimes capillary hemorrhage. The lymphatic elements undergo great hyperplasia; sometimes there is partial necrosis. In all these parts numerous micrococci have been found.

Kidneys.—An affection of these organs, shown during life by albuminuria, etc., is nearly constant. The renal epithelium is generally in a state of cloudy swelling. In severe cases the kidney is swollen, and of a uniform dark red color, being actually congested.

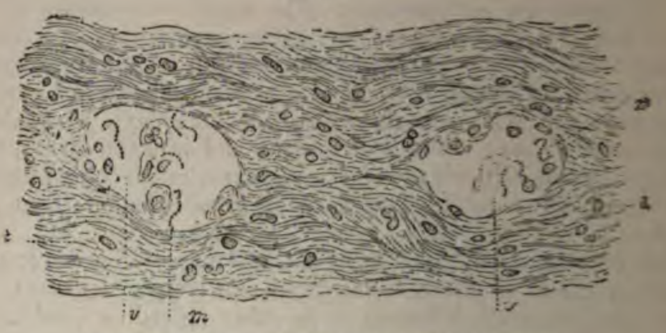
The epithelia are granular and swollen, so as almost to fill up the lumen of the tube. Minute hemorrhages are often seen. These changes are not different in kind from what are seen in other febrile complaints, but reach a high degree of intensity. Micrococci have often been found in various parts of the organ, sometimes blocking capillary vessels, or forming emboli in the Malpighian tufts. Hence the conclusion has been drawn that these are the specific parasites of the disease, which leaves the body through the kidneys; but this is doubtful, since we cannot certainly associate these micrococci with the specific cause of the disease. But it is clear that, as in the case of scarlet fever, some irritant poison passes through the kidneys.

Muscular Paralysis.—The well-known diphtheritic paralysis, beginning in the soft palate and œsophagus, but sometimes becoming very general, appears to be explained by a local action of the specific poison, first on the peripheral nerves, afterward on the nerve-centres, but its morbid anatomy is still obscure.

Erysipelas.—Doubts which formerly existed as to the existence of a specific virus causing erysipelas have been removed by experiment. It has been shown that the poison is a specific organism which may be cultivated apart from the body, and when inoculated reproduces the disease in persons previously free from it.

This has been shown even in the human subject, in cases where erysipelas has been artificially produced in order to destroy and cure a morbid growth. Inoculations of pus, or crude material from the disease, have given ambiguous results.

FIG. 78.



Section of skin in erysipelas (CORNIL and RANVIER).

v v, two lymphatic vessels, containing leucocytes and chaine of streptococcus; *t*, connective-tissue; *a*, connective-tissue cells and migratory cells. Magnified 600 diam.

The virus may, however, be received without obvious inoculation. Whether it directly enters the skin in such cases, or whether it is received by the respiratory organs and reaches the skin secondarily, is not quite clear, but the former is the more probable. Ulcers or inflammations of the mouth, tonsils and fauces are thought by some to constitute the channel by which the virus enters. Wounds from surgical operations are especially liable to be affected by erysipelas.

The incubation period, when inoculated, is from fifteen to sixty-one hours. The local affection is inflammation of the skin, tending to suppuration, and spreading locally, sometimes while the original part heals, so that it is said to be migratory. The microörganism, or streptococcus, is especially found in the lymphatic channels, at the already spreading margin of the inflammation, but it is not seen in the blood.

The general symptoms are usually very severe, in proportion to the local lesion, consisting of high fever with rigors, prostration, etc., but some cases are almost without fever. The symptoms are doubtless caused by absorption of a poisonous substance engendered in the local inflammation, since there are no secondary foci of inflammation formed.

Inoculations into the blood appear to be harmless; but in the connective-tissue and lymphatics, cause a spreading inflammation.

The virus of erysipelas may be conveyed from one person to another by direct contact, or indirectly by means of solid objects, such as the hand or instruments of the surgeon, clothes, bedding, etc. Whether it is conveyed through the air is uncertain, though, as the disease appears sometimes to be epidemic, this is not impossible. It clearly seems to attach itself to buildings, such as hospital wards.

From personal observations I have reason to believe that the virus retains its vitality in the dead body for a certain time, and that both direct and indirect communication from this source are possible. How long infectiveness remains when the virus is dried up on indifferent objects is quite uncertain.

The contagiosity of this disease is extremely variable.

It is generally thought that traumatic or "surgical" erysipelas is contagious, while the apparently spontaneous non-traumatic, or "medical" form is not so. The chief reason appears to be that most patients in a surgical ward have, while those in a medical ward have not, wounds or lesions of the skin which facilitate the entrance of the poison.

One attack gives immunity against inoculation for a few months; but, after this, persons who have once had the disease are more liable than others to take it.

Dysentery.—The claims of dysentery to be regarded as a specific disease are disputed. But its limited geographical distribution, its epidemic occurrence, and a contagiosity which is sometimes definitely proved though not universal, are sufficient to give it this character. For many years past, dysentery has been all but unknown in London and England generally, so that when cases occur, they are for the most part preferable to foreign importation.

The poison is chiefly miasmatic, residing in the soil, especially in marshy, badly-drained places, in the same situations as ague and malarious fevers, but more especially in certain parts of the world.

It is received into the body generally by water or possibly by food containing the poison. Some think that it may be received by the breath also. The local effect of the poison is seen almost entirely in the large intestine, producing inflammation, ulceration, hemorrhage, etc. The liver is often affected, probably through absorption of the poison, from the alimentary canal.

The other symptoms appear to be a consequence of the intestinal lesions, and there is no evidence of presence of poison in the blood, or its generalization through the body. It remains, however, for a long time attached to the mucous membrane, so that when the acute symptoms are over, the disease often becomes chronic, and may recur when the patient is far removed from the soil whence he originally derived the virus.

It is also clear that the poison leaves the body with the intestinal discharges, and, passing into soil or water, there preserves its vitality, so as to be capable of producing new cases of the disease. Whether the poison, in a contagious form, exists in fresh feces, is doubtful, but some physicians think it may be absorbed by inhalation, as by incautious smelling of dysentery products.

Since there is no evidence of the poison leaving the body by any other channel, dysentery is not, in the ordinary sense, contagious to those around the patient, but the disease may be propagated, like typhoid fever, indirectly.

The nature of the virus is not known. In some cases micrococci have been found; in others they have been wanting (Ziegler). Minute animals, *amœbæ*, have also been observed.

Morbid Anatomy of Dysentery.—The morbid changes may be confined to the rectum and sigmoid flexure and lower part of the colon, or may involve the whole of the colon, cæcum, and even a part of the ileum. In the first stage the mucous membrane is extremely swollen and of an intensely red color, from congestion and hemorrhagic infiltration; the surface covered with a glairy, mucous, and albuminous exudation. On section the thickness of the mucous membrane is very apparent. This condition is an intense catarrhal inflammation with interstitial exudation and hemorrhage.

In a later stage the mucous surface looks unequal and ragged, parts being raised and others depressed. The raised portions are covered with a sort of slough composed of necrotic epithelium, mixed with exudation, of a dark red, gray, or blackish color. The depressed portions are either only intensely inflamed, or else, from the falling off of the sloughs, ulcerated. The ulcers are very various in extent and depth, and of irregular shape.

Sometimes a considerable portion of the mucous membrane will appear to have sloughed off. Those portions which remain may be greatly thickened and even form polypoid excrescences. The other coats are deeply infiltrated, more rigid than usual, but at the same time sometimes more brittle, so that I have seen the bowel easily broken in removing it.

As the ulcers heal, fibrous scars are produced, which sometimes cause contraction.

Few opportunities occur in this country for investigating the minute changes. In the specimens we have seen, the mucous membrane is found to be converted into a dimly granular mass, in which the outlines of the individual elements, as well as the nuclei of the cells gradually disappear.

Beneath these necrotic masses there is a dense cellular infiltration which may extend through the whole submucous tissue and even involve the muscular coat.

The change is thus almost purely necrotic, as regards the epithelium; and in the submucous tissue shows destructive inflammation, not tending to fibrous growth, and not necessarily forming abscess.

These changes evidently much resemble those of diphtheria, and hence are called intestinal diphtheria by some German writers. Similar changes are said to be produced in certain cases by mere fecal accumulation; but such cases must be as rare in this country as true dysentery.

Tetanus.—There is some difference of opinion as to whether this is to be regarded as a specific disease. The reasons for thinking it so are:

1. It is epidemic, though not definitely contagious, and is remarkable in its geographical distribution, occurring most frequently in hot climates. 2. If occurring after a wound, it does not depend upon any specially aggravated or unhealthy condition of the latter. 3. It

runs a definite and, on the whole, typical course, accompanied by fever as well as toxic symptoms. 4. It may occur without a wound. 5. Tetanus has been conveyed to a veterinary surgeon from a wound acquired in the post-mortem examination of a horse dying of tetanus; and the disease was fatal (*Brit. Med. Journal*, March 5, 1867). 6. This or a very similar disease has been produced in rabbits by inoculating infusions of tissues taken from a wound in a case of human tetanus. The experimental disease had an incubation period of two or three days, showed marked tetanic symptoms, and was transmissible by inoculation from one animal to another (Carle and Rattoni).

It was also shown by Nicolaier that a tetanic disease might be produced in mice and rabbits by introducing a small quantity of garden mould under the skin. After an incubation of about two days in mice, or from three to five days in rabbits, characteristic symptoms appeared and the animals died in from three to seven days after the operation. After death a small quantity of pus was found at the spot of inoculation, but no changes in the nerve-centres or other organs, or in the blood.

The pus showed eminently virulent properties; a very small quantity, inoculated into mice or rabbits, producing characteristic and very intense tetanus. Inoculation of material derived from the internal organs also reproduced the disease in a few instances. A peculiar bacillus was found in the pus, which will be mentioned afterward.

From these experiments it is clear that a specific and communicable disease, apparently identical with human tetanus, can be produced in animals, both by material from cases of tetanus and from a living virus contained in the earth.

If it should be proved that this is really the same disease, then tetanus would appear to be a disease produced by a specific poison contained in the soil, and introduced for the most part into a wound; sometimes possibly by other channels. When thus introduced into the body it enters the blood, and either the original bacillus itself, or something produced by it, is carried to the nerve-centres, where it sets up the physiological disturbances known as the symptoms of the disease.

Morbid Anatomy of Tetanus.—The spinal cord has been often examined, and sometimes found to be congested or slightly disintegrated. But these changes are not constant. The conclusion is that tetanus is not strictly a disease of the cord, but that the spinal symptoms are functional and produced by the specific poison.

Hydrophobia.—Though the physiological symptoms of this disease in some respects resemble those of tetanus, its origin is very different.

The specific virus of hydrophobia is derived from dogs or other animals, (*e. g.* wolves or foxes) affected with the disease, rabies. For our present purpose it is enough to state that this is a definite and specific disease and appears in two forms—that of a raging madness, in which dogs have a propensity to bark and bite; and that of dumb-madness, in which they do not bark, and suffer from paralysis of hind legs and lower jaw.

In our experience the disease is always communicated by contact of the saliva of a rabid animal with a wounded or abraded surface. There is no evidence of its ever being introduced by the respiratory or digestive channels. There is always a period of incubation, sometimes as short as eight days, usually from one to two months, in rare cases many months or even years. After this period the wound, which will probably have healed, sometimes becomes inflamed and painful; sometimes it is unchanged. Then arises the well-known symptoms of the disease, referable to an affection of the medulla oblongata, sometimes of the medulla spinalis, sometimes of the brain.

It has been clearly shown that the contagious virus of the disease is contained in these parts of the nervous system, as well as in the saliva of hydrophobic patients. It is, however, important to remember that another disease, a sort of septicæmia, was produced by Pasteur in rabbits, by inoculation of saliva from cases of hydrophobia, and that the same disease was produced by Vulpian by inoculation of saliva from healthy people. It is characterized by the presence of a peculiar microörganism in the form of a diplococcus. These experiments confirm a conclusion arrived at in other cases that the healthy secretions or fluids of one animal may contain a microörganism which produces a fatal disease in another species.

The Specific Virus.—Putting aside these results, the following facts show the identity of the virus in canine rabies and human hydrophobia, and its distribution in the body.

The identity of hydrophobia and canine rabies is shown not only by the well-known facts of the communication of the disease from animals to man, but also by the fact, frequently verified, that products of the human disease produce rabies in its two forms of raging madness and so-called dumb-madness with paralytic symptoms, in dogs; and a similar disease in rabbits, which is shown to be the same by its power of reproducing rabies in other animals. The saliva and salivary glands of animals or men dying from hydrophobia, or rabies, contain the special virus and can communicate it to animals by inoculation. There may at the same time be the other virus or microörganism above mentioned, and may be a third virus capable of producing suppuration.

The medulla oblongata and medulla spinalis and cerebrum contain the same virus and may communicate the disease in the same way, though they do not contain the other viruses just mentioned. It is always found in the medulla oblongata, often, though less constantly, in certain parts of the other organs, and in the cerebro-spinal fluid. Peripheral nerves—*e. g.*, portions of the pneumogastric and sciatic—from rabid animals are virulent, and reproduce the disease if inoculated.

The virus from the nerve centres may retain its vitality for several weeks if decomposition be prevented.

The blood of rabid animals does not convey the disease.

Portions of the nerve-centres mixed with sterilized broth are the most certain medium for conveying the virus, and have been generally used by Pasteur.

Method of Inoculation.—The virus may be injected (1) under the skin, (2) into the veins, or (3) applied to the cerebral surface, under the dura mater, after trephining.

1. Subcutaneous injection is somewhat uncertain. It has a variable incubation-period, sometimes very long.

2. In injection into the veins the incubation period is shorter, but varies with the dose; being on an average seven to ten days.

The virus acts chiefly on the spinal cord, usually producing dumb-madness with paralysis; but furious madness may be produced if a very small quantity of virus be injected. Thus either form may be produced at will.

3. Inoculation of the cerebral surface is a very certain method. It produces in dogs furious madness, with barking and biting propensities.

In animals which have received the disease by virus from the nerve-centres, through venous or cerebral inoculation, the saliva and salivary glands are as virulent as in cases of supposed spontaneous rabies.

These experimental results conclusively prove that rabies and hydrophobia are due to a communicable virus, which when received into the body enters the circulation, and produces the symptoms of the disease by direct action upon the different parts of the nervous system, the symptoms being cerebral (*i. e.*, madness, etc.), spinal (paralysis), or peripheral (*e g.*, hyperæsthesia, which is a marked symptom of human hydrophobia), according as these parts of the nervous system respectively are affected. These symptoms cannot, then, be due to a reflex nervous action starting from the wound—a hypothesis also directly negatived by other experiments.[1]

Method of Preventing Inoculation.—Pasteur found that it was possible to render dogs incapable of acquiring rabies by the following method:

The virus from a rabid dog is inoculated through a long series of rabbits, one being inoculated in the brain from the spinal cord of another, till a virus of constant strength, and having a uniform incubation of about seven days, is obtained.

The spinal cords of rabbits dead from rabies produced by this virus are removed with antiseptic precautions and suspended in dry air, *i. e.*, in a glass bottle over caustic potash. Thus preserved they gradually lose their virulence, and are completely inert after sixteen or twenty days. A series of cords thus preserved gives accordingly an ascending series of virulency. By inoculating dogs successively with an ascending series of spinal cords thus weakened, Pasteur claims that they become insusceptible to the action of the strongest virus; and a large number of dogs thus prepared were tested by a commission and found to be insusceptible of rabies.

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[1] See report on Pasteur's Researches, by William Vignal, British Med. Journal, 1886, vol. i, pp. 671, 727, etc.

The only objection to the conclusion is the alleged fact that, though the dogs do thus acquire an immunity against the artificially treated virus used by Pasteur, they are not, or not always, insusceptible of the disease as conveyed by virus from a fresh case of rabies. This point must be considered as not yet satisfactorily settled.

Preventive Inoculation in the Human Subject.—After three years' continuous experimenting upon animals, Pasteur applied the same method to human subjects already bitten by mad dogs or wolves.

Virus from the spinal cords of rabbits, prepared as above stated, is injected under the skin in the abdomen in an ascending series of virulency; the treatment extending over ten days. It is claimed that the immense majority of cases thus treated escaped infection with hydrophobia, only one patient out of 688 dying of that disease. The usual mortality is stated to be one in six or one in four.

The great objection to these results and to the practice founded upon them is the risk that hydrophobia may be actually conveyed by the inoculations.

There is ground for this apprehension, since, in a few instances where death has occurred after inoculation, the disease has been seen in the paralytic form (*dumb-madness* of dogs), which is otherwise very rare or almost unknown in man.

The question cannot therefore be regarded as yet positively decided.

Explanation of Pasteur's Results.—The theoretical explanation of this alleged immunity conferred by inoculation of the virus, suggested by Pasteur, is as follows:

He supposes that the hydrophobia virus consists of two parts.

1. A living part, capable of multiplication, *i. e.*, an organism.
2. A secondary poison, which is the product of this organism.

The phenomena of the disease would then result from the manufacture of this secondary poison within the body, as a consequence of the growth of the organism.

Now it is a law, at least widely prevalent in the case of both zymotic and pathogenic microörganisms, that they produce substances which are in the end inimical to their own development.

Thus in vinous fermentation alcohol is produced by the yeast-fungus, but when the amount of alcohol produced reaches a certain proportion, the development of the yeast is checked. Similar facts have been, in some few instances, observed with regard to pathogenic microörganisms.

Supposing, then, that we could saturate the animal body with No. 2, the *product* of the hydrophobic poison, this would check the development of No. 1, the microörganism, so that if the process were continued long enough the latter would die and be incapable of producing its deleterious poison.

If this theoretical explanation be well founded, the effect of the successive inoculations of weakened virus is to introduce into the body so much of the poisonous *product*, in the form of weakened virus, as to prevent the development of the organized virus or *organism* in the original wound.

CHAPTER XXXVI.

THIRD CLASS OF SPECIFIC DISEASES; CONTAGIOUS SUPPURATIONS.

Diseases of which the Specific Poison is Contained in or Conveyed by Pus.—The variety of diseases which may be conveyed by unhealthy pus is enough to show that pus alone and in itself cannot be their cause, but that there must be a specific poison conveyed by it in the case of each disease.

We shall here consider:

1. Contagious suppuration of the skin, or Impetigo contagiosa.
2. Contagious ophthalmia.
3. Soft chancre, or chancroid.
4. Gonorrhœa.
5. Pyæmia.

1. Contagious Suppuration of the Skin.—Perhaps the simplest case of a specific poison conveyed by pus, is that of the inoculable pustular affection called Impetigo contagiosa.

In this, suppuration on one part of the surface of the body is conveyed by the fingers or other means to other parts, and there inoculated, producing pustules. In the same way it may be conveyed to another person, and thus constitutes a contagious affection, which spreads in houses, and especially in schools. The writer has shown that the poison may be derived not only from a preëxisting skin affection, but from other forms of superficial suppuration, such as otorrhœa, conjunctivitis, festering wounds, whitlows, and even ulcerative stomatitis; while, conversely, pus from the skin affection may cause some at least of these diseases. It affects the lymphatic glands very rapidly and certainly.

The disease is quite local—the poison does not enter the blood or infect the body, and hence one inoculation does not protect against others. Thus the affection, though contagious, is not an infective disease.

There is evidently something specific in the poison thus conveyed, for all pus is not inoculable in the same way. That from large open wounds is rarely locally contagious, though perhaps an approach to the same condition may be seen in the crop of pustules which sometimes breaks out around a healing wound. On the other hand a certain predisposition, either of age or constitution, greatly favors the inoculation. Children mostly suffer, and adults are with difficulty inoculable, though they enjoy no immunity.[1]

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[1] Payne, St. Thomas's Hospital Reports, vol. xiii. p. 301.

It is difficult to say what the nature of the poison is. Micrococci are constantly found in the pus, but do not appear to differ from those found in other suppurations, such as in boils and carbuncles. The question of the specific nature of these will be discussed later on; but in the meantime it may be pointed out that a succession of boils on the skin may be derived one from another by inoculation, like the pustules of impetigo. In both cases *pressure*, as that of clothes in certain parts of the body where boils are common, and scratching in the case of impetigo, undoubtedly favors the inoculation of the virus.

2. Contagious Ophthalmia.—It is well known that superficial inflammation of the eyes is sometimes contagious, but, on the other hand, it is very strenuously denied that it always is so. Again, its occurrence in an epidemic form, in schools, etc., may be thought to show that a special irritant is diffused in the air or dust. It seems also established that a cachectic condition of body, and youth in the patients, predispose to the disease.

I have known this affection to be produced by contagious impetigo; and also to give rise to that disease both in the same individual and in others.

These considerations, together with the fact that contagious cases appear to pass, by imperceptible gradations, into non-contagious, make it difficult to trace the path of a morbid poison from one case to another; but it is clear that, sometimes at least, the secretions from an inflamed eye possess the property of setting up a similar inflammation in others, and therefore some specific poison must be contained in them. The poison, however, never enters the blood, and hence the disease is not constitutional or, strictly speaking, infective.

3. Soft Chancre or Chancroid.—This affection supplies another instance of a locally inoculable and contagious form of pus. For the characters which distinguish it from a syphilitic sore, reference must be made to surgical works.

It has been proved by repeated experiments that the secretions from such a sore can be inoculated in other parts of the body of the patient, but do not give rise to any constitutional disease; and these sores are thus distinguished from the primary lesion of syphilis. They can also produce by inoculation similar sores in other patients.

The poison cannot be the same as that of impetigo or of gonorrhœa, since the lesions produced are different.

We have here, therefore, another instance of a locally contagious and inoculable, but not an infective, disease.

4. Gonorrhœa.—It is a well-established fact that the pus from certain urethral inflammations is capable of producing a similar inflammation in other patients, and hence we must conclude that some virus is contained in this pus. The only difficulty in adopting this explanation is, that some forms of urethral suppuration do not appear to be contagious; but this does not take away from the specific inflammations the contagious property which they possess.

The pus of gonorrhœa, if applied to the conjunctiva of the eye, produces a very severe form of inflammation, which possesses apparently the same contagious properties. It appears to be innocuous on sound skin, or even if inoculated.

In most cases the virus does not enter the circulation, and the affections remain local, like those suppurative affections already spoken of.

In some cases, however, the poison is evidently distributed by the circulation, and produces secondary lesion in distant parts.

The commonest form of such lesions is an inflammation of the joints, the so-called gonorrhœal rheumatism, the special characters of which need not be considered here. Another secondary lesion is one affecting the eyes, which was observed long ago, by Sir Astley Cooper, sometimes to accompany the joint-affection.

This is often displayed in affections of the deeper structures, or sclerotitis, and is thus readily distinguished from the results of superficial inoculation of the conjunctiva. Sometimes the conjunctiva is affected, but even then the mildness of the inflammation contrasts with the great severity of inoculated gonorrhœal conjunctivitis. Whether any other internal lesions are produced is not known.

These facts forbid us to regard gonorrhœa as a purely local affection. Since the poison can enter the blood, the disease is, to that extent, infective and constitutional. But the constitutional symptoms produced, beyond fever, are not notable.

The manner in which the poison becomes generalized is not known. Nevertheless, since the deep pelvic veins, *e. g.*, the prostatic plexus in man, are often found after death from various causes to be the seat of *thrombosis*, it is possible that the machinery of distribution is the same as that about to be described in pyæmia. But there is no direct post-mortem evidence as regards gonorrhœa.

Recent researches have made it almost certain that the specific virus of gonorrhœa is contained in a micrococcus (gonococcus) to be described later on. It is even stated that this organism has been found in the secondary joint-inflammations, as well as in the original lesion, but several investigators have entirely failed to find the gonococcus in the inflamed joints. It is possible that a suppurative virus may be mixed up with the specific organism of gonorrhœa.

5. Pyæmia.—The essential fact in this disease is that inflammation of one part of the body produces secondary foci of inflammation in distant parts.

It was at one time thought that pus was *absorbed* at the original seat of inflammation, and *deposited* in the secondary foci; hence the names "purulent absorption" and "secondary deposits." Though this is now known not to be the case, doubtless there is a transference of some morbid material from the primary focus to the secondary; and this must be regarded as a specific virus. It is possible, however, that there is more than one such virus, and that pyæmia is really the name for a group of diseases rather than one only; but everything points to the introduction of some poison from without as being the cause of the symptoms. This enters the blood and causes constitutional disturbances as well as local inflammations. It is not clear in what way it leaves the body, if it does so at all.

The evidence for the disease, or diseases, being produced by a specific poison introduced into the body from without is of the following kind:

1. The disease mostly begins with a wound, which, before or when the symptoms arose, is usually changed in character or becomes "unhealthy." The wound may, however, be very slight, and may be apparently running a normal course.

2. It affects large numbers of men at once, as in armies, or in certain hospitals.

3. The infection remains attached to certain buildings, and also to material objects, such as clothing and instruments.

4. The reception of the infection by a wound may be almost entirely prevented by preventing the entrance of a poison from without, either by antiseptic precautions or by very scrupulous ordinary cleanliness. Which of these methods is the better is a very important question practically, but not in relation to the point here considered. By such methods the disease has been, in some places where it was formerly prevalent, quite stamped out, and rendered of late years comparatively rare in all European hospitals.

5. The occurrence of pyæmia without any discoverable external wound, sometimes called "medical pyæmia," of which there can be no doubt, is also evidence in the same direction, although it has been interpreted in two ways.

(1) It has been supposed to show a spontaneous or idiopathic generation of pyæmia-poison within the body. (2) Such cases may be regarded as showing the reception of the poison by some other channel than by a wound. The writer strongly inclines to the latter view. It seems improbable, and not to be supposed without exhaustive proof, that such a disease should rise spontaneously in persons comparatively healthy. On the other hand, supposing the pyæmic poison to be diffused in human dwellings, it must from time to time enter the respiratory and digestive channels, where it will mostly be innocuous, but, in rare instances, from some accidental lesion, enter the blood and become widely distributed.[1]

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[1] Reference may be made to two cases previously described by the writer (*Trans. Path. Soc.*, xxii. p. 332), in which pyæmia occurred without external wound or injury. In one of these cases the symptoms of pyæmia were undoubted, viz., fever, etc., with suppurative arthritis of one knee-joint and cutaneous suppuration. *Post-mortem* was found a caseous (scrofulous?) gland containing putty-like matter, apparently of considerable age—weeks or months—without pus. This had softened and opened into the superior vena cava, where it produced a crumbling thrombus, from which it must be supposed that infection of the blood had taken place. There were a few *old* caseous nodules in the lung, and a very few minute *recent* abscesses also. If this caseous gland contained the poison, it must have received it from the lungs, *i.e.*, through the respiratory channels. At the time this observation was made, in 1870, no attention was paid to microörganisms. The specimen is in the museum of St. Mary's Hospital.

Morbid Anatomy of Pyæmia.—The external character of wounds which most commonly give rise to pyæmia are described in surgical works. It need only be remarked that there is generally a deficiency of healthy granulations and free suppuration, which evidently acts as a barrier to the introduction of foreign bodies. The disease usually begins suddenly with rigors, and, invariably, with fever.

The parts adjoining the wound sometimes present no marked characters, but in the majority of cases the veins are found affected. They contain clots, not normal in appearance, but pale or mottled and usually crumbling, or softening into a pulpy mass of a pinkish or yellowish color.

The softened material often superficially resembles pus, but on microscopical examination is found to consist of granular *débris*, with perhaps some shrivelled corpuscles. In rare cases actual pus has been found in the vein, and still more rarely pus has been found directly entering it.

The coats of the vein are often thickened and inflamed, especially the intima; and the mass of clot is sometimes so large that the vein appears swollen.

The explanation of these appearances appears to be that the poison from the wound passing into the veins, either from small unnoticed vessels, or by directly penetrating the walls, first coagulates the blood in the veins; and this coagulation to some extent interposes a barrier to its passage into the circulation. But in cases where general infection results this barrier is soon broken down by the softening and disintegration of the clot, which process supplies the machinery by which the poison is distributed over the body.

By means explained in the chapter on thrombosis, softened material or small fragments of clot are carried along the veins and through the heart till they reach the *lungs*, and often beyond them, into the systemic circulation. The lesions thus produced are called *secondary*.

Secondary Lesions of Pyæmia.—*Lungs.* We find blocks or infarctions, and abscesses.

The blocks resemble to a great extent the simple embolic blocks already described. They are, however, on the average small in size, not usually larger than a hazelnut, or perhaps the size of a walnut. The shape is very irregular. The solid dark-red hemorrhagic block is seldom seen; the most usual appearance being that of a yellowish crumbling mass or abscess-cavity surrounded by deeply congested red, or almost black, tissue. They are generally situated at the periphery of the lung, and the pleural surface is inflamed and coated with lymph.

The arterial branches leading to the diseased patches, if carefully examined, are almost always found to be blocked with soft, yellowish, granular material, in fact with disintegrated fibrin. This material is probably in part derived from the veins of the primarily inflamed part, being in fact an embolus; partly it is the result of local thrombosis.

The softened or puriform matter in the centre of the block is usually found to consist of necrotic material like that of a simple infarctus, mixed with pus-corpuscles. But sometimes it is actual pus, and the lesion may then be described as a true abscess. Probably necrosis is the first stage, and suppuration the second, or the degree of suppuration may depend upon the intensity of the poison.

It is plain that these appearances depend upon two factors, viz. arrest of circulation, like that produced by a simple embolus, and local necrosis and suppuration, produced by the poison which the embolus conveys.

When the abscesses are very small and the suppuration very intense, little or no obstruction may be found in the arterial branches.

In such cases the conveyed material probably causes capillary obstruction rather than true embolism, and the capillaries originally blocked are destroyed by the suppuration. General as well as local pleurisy may result from the extension of the infective process. The production of lesions in the lungs is specially characteristic of pyæmia resulting from thrombosis and embolism. But there is reason to believe that there may be also a *lymphatic pyæmia*, in which the poison passes along the lymphatics and is first arrested in the glands. Subsequently it will produce the same general infection as in the case first supposed.

The diseases included under the general term "puerperal fever" supply examples of both these processes; as in some cases thrombosis of the veins is a marked feature, in others the lymphatics are specially affected, but in both there is a general infection.

In cases of supposed idiopathic pyæmia above-mentioned there may or may not be embolic blocks in the lungs. These cases especially tend to become chronic; a febrile disease arising, of which the nature is often for a long time obscure.

General infection, and the production of multiple lesions in distant parts of the body, characterize all these forms.

Lesions of Other Organs.—Supposing the pyæmic virus, by whatever channel it may have entered the blood, to pass the pulmonary circulation, not being arrested there, or only partly, it may give rise to similar phenomena in other organs. Experiment has proved the possibility of finely divided material passing through the pulmonary capillaries and becoming arrested in the systemic. For obvious reasons the obstruction in these secondary lesions will be in capillaries, not in larger vessels, and it is seldom possible to find clots in the vessels. The lesions have, therefore, rather the character of abscesses than blocks.

Such abscesses are more often seen in the liver than elsewhere, and are there usually multiple. They may also occur in the brain, kidneys, spleen, cellular tissue, skin, etc. Suppurative inflammation of joints also frequently occurs.

It is clear that some substance is distributed by the blood which has the power of producing inflammation, and probably also of coagulating the blood.

Nature of the Pyæmic Poison.—It was thought that pus itself was the poison producing these changes, and that this entered the circulation.

But it is certain that this does not occur. The phenomena of pyæmia are explained by two processes: (1) the absorption of liquid or diffusible matters, which cause fever and the general symptoms of the disease, *i. e.*, what is called septic poisoning; (2) the entrance of the solid or minutely divided matters, which cause the local obstruction of circulation, necrosis, and abscesses.

The nature of the fever-producing substance is still uncertain. It may be one or more of the bodies called ptomaïnes described elsewhere; or it is possible that it is an albuminous substance, more of the nature of a ferment; or there may be substances of both kinds. The ptomaïne or toxine would then be the cause of fever and poisoning: the ferment of the necrosis of tissue, which is also a conspicuous feature of pyæmia (*see* Septic Poisoning, p. 311).

The solid or "particulate" matters are almost certainly micrococci, which may be associated with fragments of broken-down clot.

With regard to the connection of these two, it is possible that the micrococci produce the ptomaïnes or other diffusible poisons; or, on the other hand, that the two are independent, and that the micrococci only exert their specific influence in the presence of the other materials which are derived from decomposed tissues and fluids.

Micrococci are found constantly after death in the secondary lesions, either within the capillaries or in the tissues; but as they multiply in the dead body, the numbers present under these circumstances are no evidence that the same existed during life. They are not constantly found in the blood during life. But their presence or absence in a drop of blood drawn for examination must be largely a matter of chance.

The species of micrococci will be discussed hereafter; but it should here be stated that they appear to be the same as are found in pus from ordinary inflammations.

Their special effect in producing pyæmia would then be due either to combination with a septic poison, as above suggested, or else to their numbers, since under ordinary circumstances the micrococci of suppuration enter the blood, if at all, in very small numbers.

Septicæmia.—In some cases of pyæmia, death results from general constitutional disturbance without secondary lesions.

Such cases have been described as *septicæmia*, it being supposed that the disease is then due to the absorption of putrid matters, without any necessary participation of microörganisms. This may or may not be the case; but the term septicæmia has been used in so many senses that some explanation must be given of them: (1) As above, for the disease produced by absorption from unhealthy wounds, without secondary abscesses, etc. (2) Disease produced by the direct introduction of putrid matters into the blood. Such diseases have been often produced artificially in animals. If the condition occurs in human pathology, it is when some part of the body is in the state of putrid decomposition or gangrene. It has been proposed to call this condition, by way of distinction, *sapræmia*, or *septic poisoning*. (3) Of late years the same name has been given to a variety of artificial diseases produced in animals by inoculating, not putrid materials direct, but bacteria contained in and cultivated from them. Seven such diseases were first produced and distinguished by Koch. It is doubtful, however, whether such ever occur spontaneously in the human subject, and obviously they have not been produced by experiment in man.

With regard to these different definitions or different senses of the word septicæmia, the following observations must be made:

1. The question whether there is or is not a disease arising from wounds, which should be called septicæmia, as distinct from pyæmia is one belonging to special surgery and cannot here be discussed.

2. The condition called *sapræmia* is a form of poisoning: it does not pass from one person to another, and therefore is not a specific infective disease as here understood.

3. The artificial diseases of animals do not require consideration here; but they are, strictly speaking, specific infective diseases.

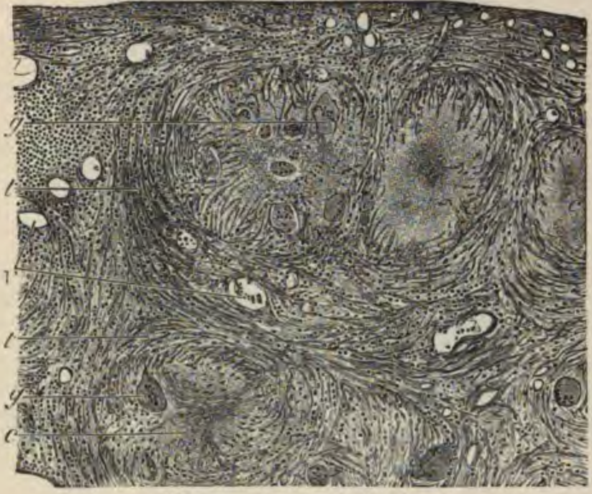
CHAPTER XXXVII.

FOURTH CLASS OF INFECTIVE DISEASES; GRANULATION-TUMORS AND ALLIED DISEASES.

IN this class the *local effects of the virus* on the tissues are the most marked feature. The products of this action constitute the so-called infective granulomata or else more acute forms of local inflammation.

The greater number of these diseases may be inoculated, and when thus introduced into the body, produce a well-marked initial lesion. The subsequent changes have, for the most part, the character of progressive inflammatory new-formations. They tend, in most cases, to become chronic, because the new elements produced are generally more permanent than those of the acute specific fevers, and because the virus is capable of retaining its vitality for a longer period in the body, and because the changes produced are more local than general.

FIG. 79.



Minute anatomy of tubercle.

The mass shows several tubercular foci or "giant-cell systems," with commencing fibrous formation; *g g*, giant-cells; *v*, bloodvessel in tissue between the tubercular foci; *t*, fibroid tissue; *c*, caseous material.

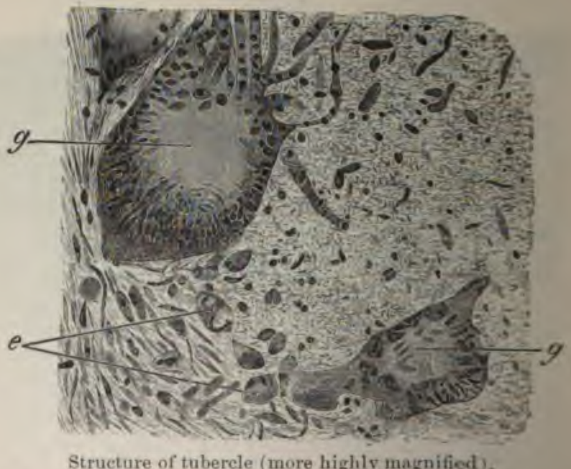
In this respect they form an ascending series, from anthrax, which is the most acute, to leprosy, which is an exceedingly chronic disease. The last-named is not actually known to be inoculable, and is not certainly contagious, but nevertheless has more affinity with this class than with any other.

These diseases are referred to in the chapters on the infective gr ulomata and on vegetable parasites, but we shall here describe th phenomena as due to the action of a morbid poison (*see* Chap XXIV.).

Tubercle.—The word tubercle means merely a small lump, and formerly used for any small growth of globular shape, but has no special sense. After much controversy, the structure known as a miliary tubercle is now regarded as the essential type of the disease

Such a tubercle is a body about one-sixteenth to one-eighth of inch in diameter, roughly globular, but looking angular on section a pearly gray or yellowish color. On section it is found to be c posed of lymphoid cells, of so-called epithelioid or formative cells, often of very large cells with many nuclei, called giant-cells: wh are arranged, speaking broadly, in the above order, passing from side inward. There is sometimes a fine reticular stroma, like tha a lymphatic gland, so that tubercle has been described as a min lymphoma; but it is not constantly found. The three kinds of are not always present; sometimes two only, sometimes lymphoid alone. Tubercles large enough to be visible usually contain sev such foci.

FIG. 80.



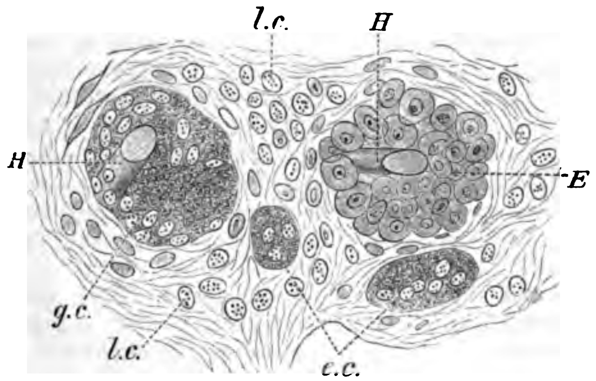
Structure of tubercle (more highly magnified).
g, giant-cells with prolongation; *e*, epithelioid cells.

This structure is quite non-vascular; the capillaries in well-injec specimens being traceable to the very margin of the tubercles, but into it, so that if vessels are ever formed they are very early ob erated.

There can be no doubt that this structure is really a product inflammation, set up by the action on the tissues of the special vi of tubercle This virus consists of a bacterium, the "tubercle-bacill which irritates the tissues, either directly or by means of the substan which result from the chemical changes it sets up. The reasons the inflammation takes a special form, which may make it difficult to recognize the process as such, have already been considered. But, in order to show that the mechanical irritation of small foreign particles may produce giant-cells and a structure resembling tubercle in animal tissues, Baumgarten, by introducing fine hairs into the cornea of a rabbit, produced the structure represented in Fig. 81, which may be called a *pseudo-tubercle.* We see the fragments of hair either embedded in a giant-cell, or surrounded by a group of epithelioid cells, the whole connected by a granulation-tissue, so as closely to resemble a tubercle. The question, how it differs from a true tubercle, is a very interesting and important one.

Briefly, we may say there are two essential points of difference between this and a tubercle produced, let us suppose, by inoculation of tubercular matter into the cornea of the same animal. (1) The pseudo-tubercle forms a small mass of fibrous tissue; a small scar, in fact, without further change. In true tubercle there is subsequently necrosis, or death of the elements, leading to caseation. (2) The pseudo-tubercle remains single, having no power of forming other similar structures. True tubercle has an infective power, producing other tubercle in its neighborhood; and if inoculated into one point may produce a series of fresh foci of disease, by which the virus is transmitted through the tissues, to other parts of the same organ, to lymphatic glands, or to distant parts.

FIG. 81.



Pseudo-tubercle, produced in rabbit's cornea by irritation of hairs (BAUMGARTEN).

H H, fragments of hair: *E*, collection of epithelioid cells round the foreign body: *g c*, giant-cell: *e c*, many-nucleated epithelioid cells forming transition to giant-cells; *l c*, leucocytes.

The cells of tubercle have thus nothing distinctive about them. Similar elements, leucocytes, epithelioid cells, or fibro-blasts, and even. though sparingly, giant-cells, are seen in granulations. But tubercle is distinguished from the structure just named by the abundance of giant-cells, by the arrangement of the elements in a nodular form; and by the tendency to necrosis.

The most absolute distinction is the presence of the tubercle bacillus, an organism which will be more minutely described in another chapter.

Inflammation and Tubercle.—Besides the special inflammation which produces the tubercle, there is always inflammation of the ordinary type in the organ affected, or it is wanting only when the tubercle is in the earliest stage. The kind of inflammation varies with the organ; thus we have tubercular pneumonia, tubercular meningitis, peritonitis, etc.

The inflammation is almost always secondary to the tubercle: but rarely the converse may be seen—that is, tubercle extends into newly formed inflammatory tissues, such as fibrous adhesions in the pleura. But this only occurs when a tubercular infection already exists.

Changes in Tubercle.—Tubercle is liable to two kinds of change or degeneration: (1) caseous; (2) fibroid.

1. Caseous, or cheesy, degeneration is a dry necrosis which begins in the tubercle itself and extends to the surrounding inflammatory products. It produces yellow, crumbling masses, formerly called yellow tubercle, or scrofulous matter, which are not peculiar to tubercular disease, though most common in connection with it. It consists of shrivelled lymph-corpuscles, granular matter, and fat. The essential cause of this change appears to be twofold: viz., deprivation of blood-supply, and the necrotic action of the tubercle virus.

Masses of caseous matter are generally met with in some part of the body of persons dying with tubercular disease; and doubtless in most cases represent a degenerated condition of true tubercle, though the converse explanation has been given, for reasons to be presently stated. The ultimate change is that the caseous mass softens, breaks down, and forms an ulcer, an irregular abscess-cavity, or a vomica, according to its situation. This change is usual in the lung; also in lymphatic glands, in bones, and less constantly in other parts of the body where tubercle occurs.

2. The fibroid change is seen especially in certain parts of the body, as in the serous membranes and sometimes in the lung. The tissues surrounding the tubercle pass into a chronic fibroid inflammation or induration, by which masses of considerable thickness may be formed. The individual tubercles shrink into fibrous nodules.

The caseous and fibrous transformations often occur in the same subject, and hence cannot be regarded as always depending upon constitutional difference; nevertheless, there are some persons whose tissues appear specially predisposed to fibroid change under the influence of chronic inflammation, and this change more often occurs in the old than in the young.

Tuberculosis is the name given to the disease caused by the introduction of tubercle-bacilli into the body. The form called *acute general* tuberculosis in man corresponds very closely with the artificial disease produced by inoculation in animals.

There is always high fever, the temperature rising to 103°, 104°, or even more; and death may be caused by the general condition, or by special organic disease. After death, fresh miliary tubercles are found in many parts, especially in the lungs, the serous membranes, the meninges of the brain; but nearly every organ is susceptible of infection.

In almost every case tubercular disease of older date is found in at least one part, in the form of a caseous degenerated mass; very often a lymph-gland is the part thus affected. In numerous post-mortem examinations made specially to test the point, the writer has only once or twice failed to find such masses; and then there had been some antecedent inflammation, *e.g.*, pleurisy. The process much resembles the generalization of cancer from a primary tumor. Since in these old masses the tubercular structure is not evident, it has been thought that any degenerated inflammatory products may give rise to general tuberculosis. However, it is most probable that in all cases these older morbid products were originally due to the tubercular virus.

Chronic tuberculosis presents a very different type. The disease may remain for a long time, or even till its termination, confined to one organ or group of organs, such as the lungs, lymph-glands, or bones.

In these the phenomena of tubercle, inflammation and necrosis may be so mixed up as to be difficult to unravel. Hence there have been many controversies as to whether the products are tubercular or inflammatory, or a mixture of both. If regarded as inflammatory, they have been called *scrofulous*—a term which requires explanation.

Scrofula.—This name, or the adjective "scrofulous," was originally applied to chronic enlargement of lymphatic glands in the neck. Afterward this and other conditions supposed to be similar were regarded as symptoms of a special disease, "scrofula."[1] This theory is hardly supported now; but certain diseases, especially what is called scrofulous pneumonia, and certain surgical affections of the lymph-glands, the joints, bones, etc., still retain the name.

Some pathologists, without admitting a disease scrofula, speak of scrofulous inflammation. This is shown in the lymph-glands by the following characters: (1) Inflammation is excited by slight causes; (2) persists when the cause of irritation has ceased to act; (3) causes permanent injury to the parts; (4) the products of inflammation undergo degeneration at an early stage.

These characters are generally referred to special properties of the tissues of the persons affected. They are vulnerable, or easily injured; the injuries heal slowly; there is little power of repair. These properties make up the scrofulous constitution or diathesis, which may be admitted without saying that scrofula is a disease.

The domain of scrofula has been of late years much curtailed; a considerable part has been transferred to hereditary syphilis, and more and more scrofulous affections are shown to be tubercular. Scrofulous pneumonia is clearly recognized to be due to the tubercle-bacillus. Nine-tenths of the affections now called scrofulous by surgeons are of lymph-glands, bones, or joints; and in very many of these tubercle occur. Latterly it has been shown that in many, if not most, such cases, tubercle-bacilli can be found.

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[1] The words struma and strumous are often used for scrofula and scrofulous: but as struma also means chronic enlargement of the thyroid, and is invariably used in the latter sense in Continental literature, there is now an ambiguity in employing it instead of scrofula.

Hence the presumption is—and some regard it as proved—that all so-called scrofulous diseases which go beyond simple chronic inflammation are caused by the tubercular virus.

Whether this be made out or no, it is certain that scrofula cannot be defined by any structural characters, but must be, if at all, by the progress and termination of the diseases thus called.

Hence, if the name be retained, it should not be employed in a pathological, but in a clinical sense, and as such is chiefly used by surgeons.

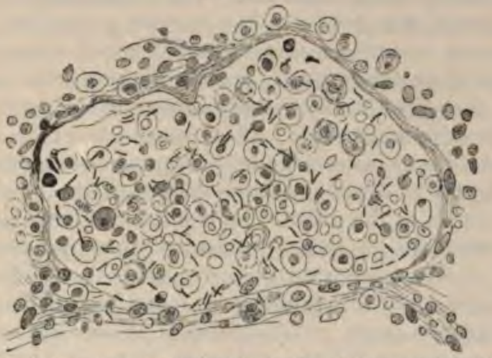
Tubercular Disease in Different Organs. Tuberculosis of the **Lungs, or Pulmonary Phthisis,** is by far the commonest tubercular disease. Here we may recognize two forms, distinguished by the manner in which the poison is introduced into and distributed through the organ. This distinction I may give in words used in 1874: "When it (tubercular disease) is associated from the first with inflammation of the bronchi and subsequent changes in the alveoli, it has the appearance characteristic of disease distributed by those channels, viz., that of broncho-pneumonia or lobular pneumonia. This will be the case whatever be the nature of the material filling the alveoli; whether it be a purely inflammatory product or something specific called tubercle. This is the *catarrhal form of phthisis.* In other cases the disease has not followed in its distribution the channels of respiration, but rather those of circulation, sanguineous or lymphatic. The tubercles are scattered through the lung, without reference to the bronchi, etc. This constitutes the *infective form of phthisis,* and agrees, in its distribution, with acute miliary tuberculosis."

We have now the advantage of knowing what the poison producing the disease is, viz., that it consists of or is generated by certain specific microörganisms called the tubercle-bacilli; and we find that in its distribution it follows the two methods above described. We have thus two chief forms of tuberculosis of the lungs: (1) Ordinary phthisis; (2) Infective tuberculosis. The forms may be combined, the latter being developed out of the former, or even *vice versa.*

1. **Pulmonary Phthisis.**—In most of these cases, it is clear that the poison enters the organ by the respiratory channels. Tubercle-bacilli are sometimes found in the sputum even before there is any recognizable organic change in the lung.

The process appears to be that the bacilli settle down in some portion of lung where there is little movement and the expulsive action of the ciliated epithelium of the bronchi is less energetic. Such a spot is clearly the apex. Or it may be in spots where previously existing inflammation favors the lodgement and growth of the bacilli. Within the alveoli and possibly in the smallest bronchioles they set up changes resulting in the formation of a miliary tubercle. It is now clearly established that the tubercle is formed at first inside the alveoli, though at one time it was thought to belong especially to the interstitial structure of the lung. The tubercle proper then becomes mingled with the products of ordinary inflammation, viz., new-formed cells derived from the lung-epithelium, leucocytes, and probably fibrinous exudation. The masses thus produced occupy the groups of alveoli and the corresponding bronchioles, so as to produce the appearance of *broncho-pneumonia.* The next and most important step is that these broncho-pneumonic masses undergo caseous degeneration, and form an amorphous or granular yellowish mass, in which all trace of the original tubercle is lost. Thus we have the commonest lesion of phthisis, which makes up a great part of the morbid changes in most phthisical lungs, viz., *caseous or scrofulous broncho-pneumonia, or catarrhal pneumonia.*

FIG. 82.



Alveolus of lung in catarrhal pneumonia, showing tubercle-bacilli (PERCY KIDD).

In this lesion the tubercle-bacilli are found by all observers to be specially abundant. When expelled into the air-passages they are probably drawn back by inspiration into other parts of the lung (as we see in hemorrhage), and set up fresh centres of infection. This process may occur alone, or may be accompanied by miliary tubercles.

Extension of the Infective Process.—The tubercular virus spreads from the alveoli and bronchioles to their walls. In these it produces, firstly, chronic inflammations. Small-celled infiltration appears around the bronchioles, the bloodvessels, etc.; and in time becomes organized into fibrous or fibroid tissue, so that the cheesy masses become surrounded by a fibrous envelope or imperfect capsule. Tubercle-bacilli are frequently found in this tissue. The fibroid change may be very extensive, and in some cases quite preponderates over the caseous, constituting fibroid phthisis. This change must be regarded as conservative. It hinders the further spread of bacilli into the tissues, and causes the process to be more chronic. In the second place the tubercular virus, like other infective poisons, causes the formation of new foci of infection like the original, that is, of new tubercles. These may be formed either in normal or in inflamed lung-tissue. The channels by which the virus passes are probably chiefly lymphatics, but possibly bloodvessels also. In this way miliary (or infective) tubercles become mingled with the caseous pneumonic masses; and this combination constitutes the ordinary form of chronic phthisis.

Since caseous pneumonia may occur without visible tubercles it was at one time thought not to be really a part of tubercular disease, but rather a form of inflammation; and a sharp distinction was drawn by Virchow and others between the broncho-pneumonic masses and tubercles. But it was evident that these changes, even if not really tubercular, were a part of the disease, pulmonary phthisis, and in 1874 the writer expressed the probable relations of these processes to tubercle as follows: "If any morbid poison should ever be shown to be the cause of tubercle, that will probably be found to produce in some cases caseous pneumonia also." This relation is now an established fact, the difference between the two processes lying in the mode in which the disease spreads. Caseous pneumonia arises from inhalation of the virus into the alveoli, while miliary tuberculosis, etc., are due to infection by bloodvessels and lymph-channels (Watson Cheyne).

Caseous pneumonia, with or without visible tubercles, may spread over a large part of the lungs, and soon undergoes necrosis. This causes softening or breaking down; the lung-tissue is thus destroyed. In all cases of tuberculosis of the lung, whatever other changes are present, this is the chief agent of destruction.

It is possible for the process to spread from the lung to other organs, but it does not often do so, except in two directions: (1) to the bronchial glands; (2) to the pleura.

1. The bronchial glands are always affected, except in the most acute cases. The changes are the same as in the original seat, ending with caseous degeneration. 2. The pleura is often affected, but sometimes escapes, even when the lung is almost destroyed. Infection takes place here also, through the lymphatics. Scattered gray tubercles appear, accompanied by inflammation and fibrous thickening.

Extension to other organs, or even to many, forming general tuberculosis, is possible, but not common. The reason, so far as understood, why the disease remains confined to the lungs, constituting a *local tuberculosis*, seems to be that the fibrous processes set up constitute a barrier to the passage of the bacilli or their virus inward, while these are constantly being expectorated with the sputa.

2. **Infective Tuberculosis of the Lung.**—If the tubercular virus be distributed by the pulmonary arterial system, it becomes arrested at various places in the capillaries, and a number of small tubercular foci are formed, which may be compared to minute embolisms. This constitutes the process known as acute miliary tuberculosis of the lung.

It may occur quite independently of any broncho-pneumonic or inflammatory process such as above described, which is proved by the fact that cases occur where the whole lung-tissue is crepitant and normal (except that it is hyperæmic) but for the miliary tubercles, and where during life the physical signs of lung tissue are absent. In children, in whom this form of tuberculosis is most often seen, it has been shown, by Buchanan and others, that the lungs may be normal to auscultation even a few hours before death, when after death the lungs have been found full of miliary tubercle.

This process may, however, be combined with the other form of tuberculosis, and it must not be supposed that in this case the tubercle is confined to the interstitial tissue. On the contrary, at an early period of growth, if not at the earliest, it forms the same corpuscular masses within the alveoli as in the other form of phthisis, together with infiltration of the walls.

This form of tuberculosis is often part of an acute fatal disease, but may occur in a more chronic form, and there becomes complicated with inflammatory changes. It is generally, if not always, combined with tubercle of the pleura, and often with the same disease in other organs.

When tubercular disease has existed for a considerable time in the lung, it will often be impossible to say in which way it originated, and especially will it be impossible to show that it originated in the infective method, for in either case, breaking down results after a time, and bacilli will be expelled with inflammatory products into the air-passages, whence they will be drawn by inspiration into the minute bronchioles of other parts of the lung, where secondary foci, of the catarrhal inflammatory form of tuberculosis, will be set up. Thus the two modes of tubercular infection of the lung will be combined.

Tubercle of the Larynx and Air-passages.—In the larynx small tubercular masses appear, which lead to ulcers. From these fresh tubercular foci are developed by infection. There is always some surrounding inflammation, so that the process may be called tubercular laryngitis.

Since the disease is nearly always secondary to tubercular disease of the lungs, the probability is that the tubercle-bacilli contained in the sputa become lodged in the folds of the larynx and set up a tubercular process there.

A similar tubercular process of the trachea may occur, but is much more rarely met with.

Tubercle of the Intestinal Tract.—In the tongue and pharynx, tubercle is rare, though not quite unknown. In the œsophagus and stomach it is still more constantly absent, but the lower end of the ileum and the large intestine are frequent seats of tubercular disease.

In the ileum the disease is submucous, beginning in the Peyer's and solitary glands. The lymph-follicles become enlarged by multiplication of small cells. They at first form grayish miliary nodules, which become opaque and yellow, and finally soften from necrotic change. The mucous membrane covering the follicles also sloughs, and thus an ulcer is produced. This becomes enlarged by the formation of fresh tubercles in the neighborhood, and thus extends beyond the lymphatic structures, so as not to correspond in shape to the Peyer's or solitary gland. It often extends round the intestine, following the course of the bloodvessels, and may produce stricture by the formation of a fibrous scar. It is usually surrounded by a zone of hyperæmia. Tubercles are generally seen in such an ulcer, and sometimes occur on the serous surface. The ulcer may perforate into the peritoneum.

Tubercular ulcers have considerable resemblance to typhoid ulcers of the ileum. They are distinguished by their more irregular shape and by extending in an annular form round the bowel. The wall is also less abrupt and often shows a gradual descent, as if by steps, to the floor of the ulcer (see p. 334).

The corresponding mesenteric glands are constantly affected, often showing tubercles, and becoming in the end yellow and cheesy.

Similar ulcerations occur in the large intestine, differing somewhat in form from the fact that they originate in the solitary glands. They form rather deep, excavated ulcers, often with a small, circular, external opening.

Intestinal tuberculosis appears to be generally, if not always, secondary to tubercle of the lungs. There is, therefore, much probability in the view that these lesions are caused by tubercle-bacilli which have been expectorated from the lung and swallowed with the sputa. This is confirmed by the results of experiment, which show that feeding animals with tubercular sputa, or portions of tissues from tuberculous persons, produces intestinal tuberculosis, just as the inhalation of tubercular products causes pulmonary tuberculosis. Whether infected food can produce intestinal tuberculosis in the human subject is not known.

Tubercle of the **liver** is met with chiefly in the miliary form occurring in the course of acute miliary tuberculosis. More chronic forms are rarely seen.

Tubercle of the **kidney** occurs in two forms: (1) In general tuberculosis it is not uncommon to find miliary tubercles scattered through the organ, but chiefly in the cortical substance. The virus producing them had evidently been conveyed by the blood.

(2) In the second form we find tubercles associated with caseous matter and with inflammation of the pelvis and calyces. By this process the kidney is gradually destroyed, ragged cavities being formed which open into the pelvis and ureter, and from which pus and necrotic material pass into the urine.

This form has been called scrofulous kidney and scrofulous pyelitis, but is better called *renal phthisis*, from its analogy with phthisis of the lung. It would seem as if the process began in the hollow part of the kidney, with tubercular pyelitis; but this may be a misleading appearance, and it may start, like the other form, with tubercles in the substance of the organ. Further research is needed to establish this point.

Tubercle of Brain.—(1) Chronic tuberculosis. In the brain the original tubercles attain a larger size than in other parts; lumps, from the size of a pea to that of a walnut or more, being sometimes found, not obviously made up of smaller masses.

They are generally, if not always, yellow and caseated, miliary tubercles being sometimes traceable at the margin; and they are probably, in most cases, produced by an agglomeration of miliary tubercles. This so-called "solitary tubercle" of the brain is not always associated with tuberculosis of other organs. Sometimes, but not very often, there is miliary tubercle of other parts of the brain or of the membranes.

(2) Scattered miliary tubercles of the brain-substance are sometimes found associated with a similar tubercular process of the meninges.

Tubercle of Serous Membranes.—On these surfaces tubercle always appears first in the form of gray, rather translucent, miliary tubercles. To these is added fibrous growth, in the form of cords and nodules, together with diffuse thickening of the membrane. In the peritoneum gray masses, up to half an inch thick, may sometimes be found, consisting of an agglomeration of miliary tubercles.

Caseating change is very rare, and ulceration does not occur. If the process is very rapid, the tubercles are formed without much exudation or ordinary inflammation; but in less rapidly fatal cases the latter process is also seen, forming *tubercular peritonitis*, etc. But in the pleura it is sometimes evident that inflammation precedes the formation of tubercle. *Tubercle of the pia mater of the brain* is a very important disease, which, with its accompanying inflammation and exudation, is rapidly fatal. It occurs chiefly in children, and mostly at the base of the brain; less commonly on the vertex, forming in both situations *tubercular meningitis*.

The miliary tubercles are well studied in the transparent membrane. They are mostly situated round the small vessels, especially the arteries, and often at a bifurcation. Giant-cells are not often seen, but tubercle-bacilli have been found.

Tubercle of the Lymph Glands.—The lymph-glands in connection with tubercular organs are constantly affected, showing original tubercle-structure as well as caseous masses. Tubercle-bacilli are sometimes very numerous. An apparently primary affection of lymph-glands is also not uncommon, and all stages of the process which ends in caseation, have been traced. It is, therefore, very probable that what are generally called scrofulous glands are orignally tubercular. It is at all events certain that there is no external criterion by which the one can be distinguished from the other.

In such cases it must be supposed that the bacilli have entered the mucous or other surface of a part in connection with the lymph-gland without producing any noticeable inflammation, and have been conveyed along the lymphatic vessels.

Tubercle has been found in the thoracic duct in cases of general acute tuberculosis.

Tuberculosis as a Specific Disease.—It will be well to sum up the reasons for regarding tubercle as the result of a specific virus introduced into the body, becoming distributed in it, and passing out to continue its further existence elsewhere.

Before the bacillus now known to be the cause of the disease was discovered, it was shown by Villemin and others that by introducing tubercular matter from human lungs, or other parts, under the skin of rabbits and guinea-pigs, general miliary tuberculosis of internal parts was, after some weeks, produced. Doubt was thrown upon these results by the experiments of Wilson Fox, Burdon Sanderson, and Cohnheim, who found that they could produce tubercle in the same animals by introducing neutral substances in the same parts, and setting up a chronic inflammation, that is, by continued irritation without any specific poison. But it has since been shown that in such cases the animals received the infection from the places in which they were kept, the experimental wound serving as a place of entrance for the virus. Cohnheim, by introducing tubercular matter into the anterior chamber of the eye in rabbits, was able to watch the development of tubercle through the transparent parts, and found that the tubercular growth began after an incubation period of about twenty to thirty days. These experiments have been repeated on a very large scale by Koch, Baumgarten, and many others, proving beyond doubt that tubercle is an *inoculable* disease.

Another step was to show that the infection could be received by the breath, and it was found by Tappeiner and others that tubercular sputa mixed with water in the form of a spray and inhaled, produced tuberculosis in the animals experimented upon—mostly goats and dogs—the lungs and bronchial glands being chiefly affected.

Further it has been shown that the virus may be absorbed from the digestive organs by feeding various animals with portions of tuberculous organs, or by introducing such materials direct into the intestine by operation, in order to avoid the destructive action of the gastric juice. It was found that in about half the animals experimented upon, tubercular disease of the mesenteric glands and intestine resulted after an incubation of about one or two months. Herbivorous animals were most easily affected, carnivorous least so; a remarkable fact, as if animals accustomed to eat flesh had some power of resisting infection conveyed by it. Accidental swallowing or consumption of tubercular sputa by chickens, dogs, and cats has also produced the disease; while calves and pigs have acquired it by feeding on the milk of tubercular cows or eating the flesh of tubercular animals. In experiments it has been found that the disease is conveyed to animals with most difficulty by human tubercular products, and that in general any race of animals is most easily infected by products derived from its own species.

The above results, showing the reception of the specific virus by three channels, are quite independent of any views as to the nature of the virus. But when Koch showed that the tubercle-bacillus was the cause of the disease, the question entered on a new phase. The above experiments have been repeated with pure cultivations of the bacillus grown apart from the body, and in every case with similar results. Bacilli injected into the eye produce miliary tubercle, the growth of which may be studied; injected into the veins produce general tuberculosis with perfect certainty and great rapidity; injected into special organs produce local tuberculosis of those parts; and inhaled with spray set up tubercular disease of the lungs. The difference is that bacilli produce much more constant results, seldom or never failing, though some animals, as dogs and rats, require larger doses of the bacilli than others; and feeding experiments have been less successful.

Identity of Human and Animal Tubercle.—Before applying the above results to human disease it is necessary to consider whether the tubercular diseases of animals are really the same as the disease in man. The inoculated diseases must necessarily be considered as the same, since they may be derived from human tubercle, and their anatomical characters are identical. The spontaneous tubercular diseases of animals present some points of difference. In cattle there is the so-called pearly disease, with respect to which there has been some controversy, but which is now generally regarded as tubercle, since it shows the bacillus. Dr. Creighton, on the other hand, regards it as different, and thinks it is communicable to man as a distinct disease. But even if so, it is probably rather a variety of tubercle than entirely different. Of the other animal diseases we can only say that very many species of mammals and birds are subject to tubercles which appear to be the same as the human, since they contain the same bacillus.

Summary.—Taking all the above results, we cannot doubt that tuberculosis is a specific infective disease caused by a specific virus which may enter the body by a wound, or by the respiratory, or by the digestive channels; that is to say, it combines the modes of infection which obtain in several diseases—for instance, in smallpox, scarlatina, and typhoid fever—though reception of tubercular poison through a wound is very rare in man, if indeed it ever occurs. The only known instance is the production of warts containing tubercle-bacilli on the hands of those who make post-mortem examinations.

Referring to the effects of morbid poisons as classified on p. 321, we may say that the *initial lesion* produced is a miliary tubercle, at whatever point the virus enters the body.

Generalization is shown by the production of fever and cachexia, as well as by secondary local changes.

The *secondary local phenomena* are formation of miliary tubercles, with necrosis and inflammation of surrounding parts.

The virus *leaves the body* with the discharges from the organs affected, more especially in sputa from the lungs, also in intestinal and rarely in urinary excretions. It is sometimes contained in the secretions of glands, such as the mamma and the testicle, but probably only when those organs are tubercular.

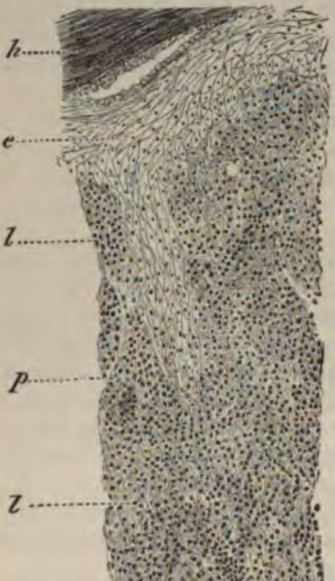
When outside the body the tubercular virus preserves its vitality and is probably carried about with dust, but there is no evidence of its growing and multiplying in these circumstances.

Is Tubercle Contagious?—The question whether tubercular disease can be transmitted from one person to another is a difficult one. Briefly, the answer seems to be that there is no clear evidence of its being in the ordinary sense directly contagious from one person to another, but it seems impossible to doubt that one case may give rise to others by indirect transmission. One argument in favor of this conclusion is that in several parts of the world savage nations who were originally quite free from tubercular disease have rapidly acquired it after mingling with Europeans.

LUPUS.

Lupus vulgaris vel tuberculosus.—This is a local disease of the skin, occasionally affecting the mucous membranes. It produces masses of granulation-tissue, in which, as in tubercle and syphilis, are collections of leucocytes, especially round the vessels and larger cells, mostly of the epithelioid type, with occasional giant-cells.

Fig. 83.



Section of skin from a lupus-patch. *h*, horny layer of epidermis; *e*, Malpighian layer; *p*, interpapillary prolongation; *l*, granulation-tissue; *g*, giant-cell (about 200 diam.).

Examining a section of skin from a lupus patch, we find the epidermis thickened with overgrowth of the Malpighian layer, from which proceed enlarged interpapillary processes. These are sometimes so considerable as to give the impression that the growth is chiefly epidermic. But below this is a vascular granulation-tissue occupying the papillary layer of the corium. It is composed of small granulation-cells and fibres, with some giant-cells. This is the structure of the soft, gelatinous-looking masses seen on the surface. It shows a transition to fibrous tissue where cicatrization is taking place.

These appearances clearly point to the influence of some persistent irritant, as in other diseases of the same class; and, in fact, a bacillus has been found in lupus, which is generally regarded as the tubercle-bacillus. This bacillus is, however, not always found, and, when present, is so in very small numbers. Hence, it is difficult to understand how, by *direct* irritation, the bacilli alone could give rise to such considerable inflammatory products. No generalization of the lupus process to other parts of the body ever takes place. It is even doubtful whether it spreads to the neighboring lymphatic glands. These are sometimes affected with tubercular lesions, but it is not clear that this affection is *subsequent* to the occurrence of lupus of the skin.

The majority of pathologists regard lupus as a local tuberculosis of the skin, and for the following reasons:

The elements of the new-growth are the same, though differently arranged.

Tubercle bacilli are found, if not commonly.

The clinical characters of the disease—progressive, destructive, and incurable, except by removal of all diseased tissue—are like tuberculosis.

Lupus is clearly traced, in some cases, to arise out of ulcerated scrofulous glands, which, according to later researches, are themselves produced by the tubercular virus.

Lupus is said, by some, to be very frequently associated with scrofulous or tubercular processes, so that in common medical parlance it is spoken of as a scrofulous disease. Actual coincidence with pulmonary tuberculosis is not common, but has been observed. The proportion of cases with scrofulous or tubercular antecedents is given as thirty or fifty per cent. or more.[1]

Inoculation of material from lupus into animals has, in many cases, produced a true acute tuberculòsis, identical with that produced by inoculating tubercle-material, as has been shown by Cornil and Leloir, Koch, Doutrelepont, and others.

Objections.—On the other hand it is urged that—

1. The anatomical structure is not precisely the same, miliary granulations not occurring, at least generally, in lupus; while the latter is much more vascular than tubercle.

2. Lupus does not undergo caseous change, though there is necrosis leading to ulceration. Fibrous induration (producing a keloid scar) is commoner.

3. Secondary infection of lymphatic glands is not very often observed.

4. True lupus has not been produced experimentally in animals.

5. There is a tubercular skin-disease which is different.

6. The actual coincidence with scrofulous or tubercular disease is denied by many. On this point, only conclusions drawn from a large number of cases can have any value. If it be admitted that the majority of lupus patients have no other disease, this, should lupus be

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[1] Three recent collections of statistics place the proportion of cases with other tubercular affections much higher. One series of 144 cases gave 79 per cent., a second series of 105 cases 62.8 per cent., a third series of 159 cases 62 per cent., while 23 per cent. in the second series and 33 per cent. in the third series had hereditary tubercular tendencies (Baumgarten, Jahresbericht über Mikroörganismen for 1886).

tubercular, amounts to saying that there is tuberculosis of one organ only—a not uncommon case in undoubted tubercular disease.

The conclusion appears to be that the virus of lupus is probably the same as that of tubercle, though the differences in the mode of action are not as yet accounted for.

Lupus exedens is a name given to severe cases of lupus, in which there is much destruction of tissue.

Lupus erythematosis is an inflammatory disease of the skin, which produces some superficial destruction, but has probably no connection with lupus vulgaris.

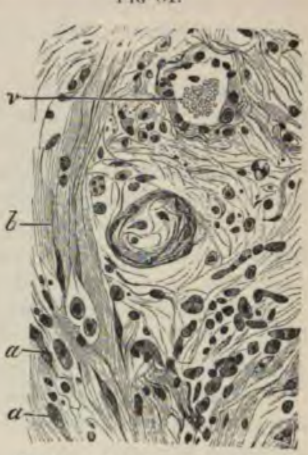
CHAPTER XXXVIII.

THE INFECTIVE GRANULOMATA—(*Continued*).

Syphilis.—This is a perfect type of an infective disease, produced by a virus introduced from without, which first sets up local changes, and then becomes distributed over the body, giving rise to a general disease and to scattered local disorders in the skin and elsewhere. After the general disease has apparently subsided, local affections may remain or appear anew, from portions of the virus which have become lodged at certain spots, and of which the activity is roused up by some cause not always traceable.

The nature of the syphilitic virus is not positively known, but from its power of reproduction within the body and communicability to other persons, it is clearly some living poison. There is no evidence that the poison can preserve its vitality outside the body except for a short time. It is not communicated by the respiratory or digestive channels, but always enters the body by some lesion of the surface. It may also be transmitted by direct inheritance from either parent.

FIG 84.



Section of primary syphilitic sore —*a*, epithelioid or formative cells; *b*, thickened connective-tissue fibres; *v*, vessel containing blood (about 300 diam.)

A bacillus has been found by some observers (Lustgarten), but it is not proved that this is the cause of the disease.

The anatomical changes produced by the syphilitic poison resemble those of other inflammations, but are limited to definite foci, and are distributed in a special manner.

The original spot of inoculation shows the so-called primary sore, or Hunterian chancre—an ulcer usually distinguished by its hardness, the external characters of which are described in surgical books.

When examined histologically, it shows inflammation of the corium, with production of numerous round cells (leucocytes), some formative or epithelioid cells, and sometimes giant-cells, but the latter are rare.

The hardness depends upon thickening and hardening of the connective-tissue fibres, as well as on new formation of tissue. The structure has not the definite form of tubercle. It is much more vascular than the latter, admitting, in suitable cases, of being pretty fully injected. However, it causes destruction of the skin and forms an ulcer. From this point the infection spreads to the neighboring lymphatic glands, which are characteristically altered. Inflamed lymphatic vessels can sometimes be traced from the original source.

After this, the poison becomes generalized in the body and sets up a general disease, usually with fever. In the course of this, in about six weeks or some months, an erythematous or papular eruption appears on the skin, which corresponds to the *rash* of the exanthemata, and, like that, may be wanting.

After this, more pronounced lesions occur on the skin, mucous surfaces, etc., which have the character of limited local inflammations and may completely disappear. Lymphatic glands in other parts of the body, sometimes very generally, undergo the same indurative inflammation as those connected with the primary sore.

The lesions already spoken of are usually called ***secondary***.

Later on, masses called *gummata* may be produced, consisting of new cells, which undergo necrosis.

These lesions are usually called *tertiary*; but it is difficult to draw a clear line between the two classes. Generally speaking, the earlier lesions are symmetrical, vascular, and may disappear without causing any notable destruction of tissue. The latter are, as a rule, unsymmetrical and irregular in distribution, and, destroying the tissue, leave a gap only partly filled up by a dense fibrous scar. On the surface deep depressions are thus produced; in internal parts, contracting cicatrices, which may, in such organs as the liver, cause great deformity.

The period of occurrence of the destructive or tertiary lesions is much influenced by nutrition; being earlier in cachectic persons. They are seen only in a minority of cases, and are sometimes set up by a mechanical injury. It must be supposed that they are due to a residuum of syphilitic virus not eliminated or destroyed.

It is characteristic of syphilitic lesions to be discrete or limited, not diffuse. General superficial inflammations, such as bronchitis, urethritis, etc., are not the consequence of syphilis.

The general histology of syphilitic products is very uniform, though influenced by situation. Apart from the primary sore, they may be considered in two groups: (1) superficial lesions; (2) gummata.

1. Superficial syphilitic products on the skin and mucous surfaces are essentially inflammations, in which the most notable feature is a collection of round cells or leucocytes about the vessels. If the eruption is more permanent, we find also formative or epithelioid cells like those in granulation; and, sometimes, giant-cells. The occurrence of the latter is very irregular, and does not seem to be connected with any particular form of lesion. Another very general feature is *pigmentation*. The brown pigment is sometimes contained in leucocytes, sometimes in fixed connective-tissue cells. In the latter case it is more permanent. Doubtless the original source is from extravasated blood-disks.

These changes are chiefly seen in the corium, but the deep layers of epidermis may be infiltrated with cells, and the change may spread to the subcutaneous tissue.

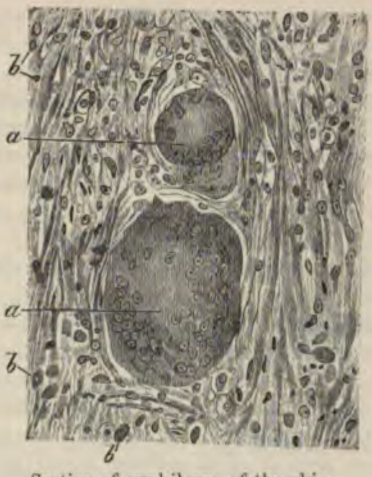
The other structures of the skin are chiefly affected passively, being infiltrated, and it may be destroyed, by the inflammatory cells; but sometimes overgrowth is seen. In moist parts of the skin—*e. g.*, the anus or genitals—the epidermis is increased, in the form of a wart, condyloma, or mucous patch. Similar structures occur on the fauces, etc.

When these changes occur in the more diffuse form, they produce the erythematous, macular, and sçaly forms of cutaneous syphilis. When they are more limited, or concentrated round some structure, such as a hair-follicle or gland, they produce the papular form called syphilitic lichen or acne. When a more considerable mass of tissue is produced, it is called a syphilitic tubercle, which is hardly distinguishable from a small gumma. What is called syphilitic lupus is of this kind.

The amount of injury caused by these lesions is proportionate to the intensity of the inflammation; and the differences between the different lesions are only matters of degree.

2. **Gumma or Syphiloma.**—This name is given when the mass of inflammatory tissue is considerable, and arranged in the shape of a tumor. . Although the process is essentially the same as in the other kinds, there are some special features. The mass, when newly formed, is composed of yellowish, somewhat translucent material, looking almost gelatinous, or gummy (hence the name), but of firm consistence. In a later stage it is opaque, yellow, and almost cheesy, but tough and not crumbling. Later on, the outer portions become fibrous, and the

FIG. 85.



Section of syphiloma of the skin.
The structure is chiefly fibrous, with many nuclei and epithelioid cells.
a, giant-cells; *b*, epithelioid cells.

appearance of a capsule is produced. Finally, the central portions become absorbed and removed either by insensible changes, or more rarely by softening and liquefaction. When the gumma is superficial a deep ulcer may be produced; when in the interior of a solid organ a sort of imperfect abscess or cavity may be produced, though rarely. Generally, a mass of scar-tissue is the ultimate stage of a gumma.

Histology of Gumma.—The greater part of such a mass is made up of what is generally called fibro-nucleated tissue; that is, of small cells or nuclei with a variable amount of stroma. The objects which look like nuclei are probably wasted and shrivelled leucocytes. Sometimes the stroma has the appearance of a lymphatic or cystogenous tissue, and this appearance was once thought characteristic of syphiloma; but it is not constant, and is mostly seen after special modes of preparation. Epithelioid cells are constantly, giant-cells sometimes, seen.

The central portions of a gumma, if not quite recent, show no definite structure, but consist of a granular or homogeneous material. The outer portions show more perfectly formed fibrous tissue, and are vascular. The other parts show few or no bloodvessels. Appearances like obliterated vessels are sometimes seen. Though the earliest stages of gumma are not often seen, there is reason to think that it generally begins with growth in and around the smaller arteries, as may often be seen in syphilitic masses from the brain. The final necrosis of the mass would then be due to total arterial obstruction.

Distribution.—Gummata occur in bone, and especially periosteum, in muscle, in the brain and its membranes, more rarely in the spinal cord and nerves, in the tongue, but rarely in any part of the intestinal canal, except the rectum; in the liver, occasionally in the pancreas, very rarely in the spleen. They occur in the kidney, and more commonly in the testicles; in the mamma very rarely. The lungs occasionally show syphilitic products, varying in tone and degree; the heart, occasionally solid gummata. In the skin, superficial gummata constitute the tubercular ulcerating syphilide.

Of these, two forms require special notice, viz., gummata of the liver and the brain.

Gumma or Syphiloma of the Liver.—This is more often met with unexpectedly after death than diagnosed during life, and is, therefore, generally in a late stage of development. It appears as a mass of tough, yellowish, opaque material, of varying size, up to some inches in diameter. The central portion is sometimes crumbling, and I have, in one or two cases, seen it of a softness equal to that of pus. The outer portions are firm and fibrous, and generally the softer the inside, the harder is the outside. The fibrous tissue is translucent in thin sections, an appearance due to the rarefaction of the liver-tissue; the hepatic cells becoming wasted and disappearing, while the *tela conjunctiva* remains, and nodules of fibrous tissue may be seen forming outside the visible mass. Thus the essential process appears to be an infiltration and destruction of the liver-tissue by a chronic inflammation, the products of which undergo necrosis. But it is probable that a an earlier stage the mass is more homogeneous, and that the central necrosis and peripheral fibrous formation occur later.

Sypiloma of the liver is generally regarded as a late product of syphilis, but probably occurs earlier than is supposed, since, unless very large, it produces no symptoms.

A diffuse fibrous change, like cirrhosis, is also attributed to syphilis; but the histological process appears different from that of ordinary cirrhosis.

Gumma or **Syphiloma of the Brain** is generally found at a late period of the disease, but sometimes earlier. I have seen it, in one case, within two months of the primary affection. The mass is a part more or less gelatinous in appearance, afterward cheesy. It is generally situated superficially, involving the pia mater, sometimes the dura mater, either at the base or on the vertex of the hemispheres. From the meninges an irregular mass extends into the brain-substance, sometimes roughly spherical and an inch in diameter, or larger. Central masses, unconnected with the membranes, are much rarer. A notable feature is the implication of the arteries. Externally they show inflammatory and hyperplastic changes in the outer coat (periarteritis syphilitica), often localized at one spot so as to produce a small tumor. The internal coat of the arteries is also inflamed (endarteritis), producing masses of small-celled growth, which narrow or block up the artery after producing thrombosis. This is doubtless one of the chief causes of the necrosis of the gumma, and in the brain may be the direct cause of death. These arterial changes appear to be the means by which, in the brain, the syphilitic process spreads. Similar changes probably take place in other visceral gummata, but from the structure of the organs are less noticeable.

Syphilis of the Lung appears in the form of inflammatory nodules varying in size, which, in the early stage, much resemble lobular pneumonia. They undergo fibroid degeneration, and considerable fibrous masses may be thus produced; more rarely a yellowish lump, like a gumma of the liver, results. The symptoms much resemble those of tubercular phthisis, and the affection may be sometimes recognized clinically by such symptoms being completely cured by appropriate treatment.

RHINOSCLEROMA.

Rhinoscleroma is an extremely rare disease, of which only one authentic case has been reported in this country. It forms masses of granulation-tissue in the nostrils, extending to the upper lip, and to the pharynx and fauces, sometimes still more deeply. The masses are extremely hard, but in structure have a considerable resemblance to lupus, being chiefly distinguished by the large size of some of the formative cells of the granulation-tissue, and by their containing colloid matter. There are no giant cells. The elementary fibres of the corium or corresponding tissue are greatly thickened, and in one case which I have examined this appeared to be the cause of the hardness of the tissue. It is a locally destructive affection, not known to become generalized.

This disease is apparently caused by a bacillus which is constantly found and has been cultivated, but not successfully inoculated. It is certainly distinct from the tubercle-bacillus. (*See* Frontispiece.)

The geographical distribution of this disease is very remarkable. It has been seen only in the eastern part of the Austrian Empire, in Italy, Egypt, and South America.[1]

LEPROSY.

This terrible disease is marked pathologically by the production of granulation or chronic inflammatory tissue in various parts of the body, but most notably in the skin or mucous membranes, and in the connective tissue of nerves. On this distribution depend the clinically recognized forms of the disease, viz., (1) tubercular or cutaneous, and (2) nervous or anæsthetic. There are also mixed forms.

In the first form, after the appearance of a macular, exanthematic eruption, lumps or diffuse infiltrations of the new growth are formed, which produce the characteristic deformities of the disease. In the second form the various remarkable symptoms produced may also be referred to the same process affecting the nervous system.

The structure of what may be called the leprous tissue is as follows: It is composed essentially of cells which at first are roundish and identical with leucocytes imbedded in a scanty fibrous stroma. These cells increase in size, till they may attain four or five times the dimensions of a leucocyte. The nuclei also become larger, sometimes many nucleated cells are seen. The cells are pale, not granular, generally roundish, rarely spindle-shaped, and sometimes contain vacuoles.

It is thus a regular granulation-tissue, in which the only special feature is the presence of large cells, which have been called leprous cells.

This tissue originates in the corium, and does not infiltrate the epidermis; it does, however, spread into the subcutaneous tissue.

The tissue is vascular and extremely persistent. It may ulcerate, but does not undergo general necrosis. Complete involution of a tuber is rare, and spontaneous cessation of the disease is unknown. The leprous virus and its products possess, therefore, a more persistent vitality than those of syphilis, or even those of tubercle.

The specific virus of leprosy appears to be a bacillus which is constantly found, and in very large numbers. These bacilli are contained in cells, and especially in the large leprous cells, the special characters of which appear to be owing to them.

They are found in every part of the body where the leprous tissue occurs, and in all cases from all parts of the world. They have been isolated, and to some extent cultivated. Inoculation into animals has produced local new-growth, but not any general disease, probably because no species of animal has been found liable to the malady. It cannot therefore be positively proved that the bacillus causes the disease, though from its constant occurrence in such great numbers it is hardly possible to doubt this.

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[1] For figures and description see paper by Sémon and Payne, Trans. Pathol. Society of London, vol. xxxvi. p. 73, plates iv. and v.

Leprosy is thus a specific infective disease; but in what way the virus enters the human body is not yet clear. Opinions differ as to its contagiousness; but it is quite certain that it may spread rapidly when introduced into a country previously free from it; and that it does not arise *de novo* in countries where it is not habitually present. The question of contagion is difficult of decision on account of the long period of incubation—extending over months or even years—which leprosy probably goes through.

GLANDERS AND FARCY.

These are two forms of a disease affecting horses and asses, one a disease of the nose, the other of the skin. Both are sometimes transferred to the human subject. It may be inoculated into some other animals—goats, sheep, etc. In glanders we have an inflammation of the mucous membrane of the nose, like a purulent catarrh, but accompanied by the formation of nodules or granulations which break down and form considerable ulcers. The ulceration may extend deeply and destroy the bone. The disease spreads to the lymph-glands (hence the name glanders) which become inflamed and then undergo caseous degeneration. Thrombosis often occurs, and there may be metastasis to the lungs and other parts.

Farcy of the skin is generally a chronic affection, in which cutaneous or subcutaneous nodules are produced, and with secondary infection of the lymph-glands. It sometimes passes into glanders.

In man the disease is nearly always acute; the formations pass rapidly into suppuration; abscesses are formed, and the whole has a great resemblance to pyæmia.

Chronic farcy in man is excessively rare, but does occur.

The anatomical structure of the nodular masses in both forms is the same, consisting in a small-celled granulation-tissue, prone to suppuration, but also forming fibrous scars. The nodules or tubercles in the acute form vary from the size of a miliary tubercle to that of a pea; in the chronic form they are larger and resemble lupus. They degenerate into tough yellowish opaque masses more like gummata.

The natural history of this disease clearly shows it to be a specific infective disease due to a living virus, and lately a bacillus, which appears to be its cause, has been discovered by Babes, Löffler, Schutz, and Israel.

It has been cultivated and inoculated into animals, *i. e.*, rabbits, guinea-pigs, as well as into horses—with the result of reproducing the disease.

ANTHRAX.

Synonym: **Splenic Fever, or Malignant Pustule.**—This is primarily a disease of cattle, derived by them, either directly from the soil or from other cattle by indirect methods of contagion.

The poison is known to be a special form of bacillus, which, when introduced by respiration, with food, or by some abrasion or slight wound, into the blood of cattle, becomes widely diffused in their bodies, producing a severe constitutional disease, often fatal, which may occur in epidemics or sporadically.

The bacillus is contained in the secretions as well as in the blood and is still active after the death of the animal. It retains its vitality for a long time, even many months after being dried up. Hence a diseased animal supplies many products by which the poison may be returned to the soil, especially if it be buried there.

In this way pastures may become permanently affected, and in countries where the disease is common such localities are well known and dreaded. The chief favoring condition in the soil appears to be moisture, and thorough drainage appears sometimes to destroy its infectiousness.

The poison may also be conveyed from one animal to another by numerous indirect methods, such as by the bites of dogs which have fed on the carcasses of infected animals, by flies, especially such as gad-flies, if they have been in contact with the blood or secretions of infected animals; also by fodder, litter, utensils, etc., which have been similarly infected. The mould of pastures retains the poison with great tenacity. Putrefaction of the carcass, and contact with putrefying substances, weaken or destroy it.

The hide, horns, and hoofs of animals that have died of the disease may transmit it; and so, it is said, may the bones, if used as manure.

Horned cattle are most liable to the disease; next sheep and horses and herbivorous animals generally; omnivorous animals, as swine, are much less liable, and carnivorous, especially dogs, least of all.

The miasmatic disease is rare in this country, and hence cattle are comparatively seldom affected. Still more rarely does it affect men; and this occurs almost always from infection through hides, fleeces, or other parts of animals brought from districts where it is prevalent.

The human disease is generally produced by inoculation, though in the countries where the cattle-disease is prevalent, infection by the respiratory and digestive tracts is not unknown.

When inoculated it is naturally almost always seen on the unprotected parts of skin, viz., hands or face, of those who have had to deal with infected materials. The poison may also be conveyed to man by flies.

Inoculation may take place by a wound, or, without that, by a pustule. A local affection is first produced which is described in surgical works as *malignant pustule*. That the disease is, for a time, local is shown by the fact that surgical treatment may completely eradicate it. But the poison usually enters the blood and produces a general disease.

Contagion from man to man very rarely occurs, but a few cases have been recorded. Inoculation of blood or fluids from infected persons will, however, reproduce the disease in animals. Infection has been known from post-mortem examinations.

We have, therefore, in this disease a perfect example of a specific poison which may pass from the soil to an animal body, these undergo an enormous multiplication, and, after passing through one or several bodies, return to the soil again, preserving its infective properties. A disease thus perpetuated is both miasmatic and contagious.

Although in some respects very different from tubercle and syphilis, anthrax agrees with the infective granuloma-diseases in the fact that the inoculation produces a severe initial lesion before generalization of the virus takes place.

CHAPTER XXXIX.

FIFTH CLASS OF SPECIFIC INFECTIVE DISEASES; MIASMATIC DISEASES.

THESE are diseases of which the poison exists in the soil or water and is thence taken into the human body. There is no evidence as to the way in which the poison leaves the body, if it does so at all. Hence communication of the disease to other persons by the ordinary channels is unknown or very rare.

It follows that a person acquires a miasmatic poison by sojourning in a certain place; but he may carry the poison away with him, and become affected by it either at the time or after a period of incubation.

It should be borne in mind that there are some diseases which may be acquired both from the soil and from other persons; that is, which are both miasmatic and contagious.

Pure miasmatic diseases are ague and other forms of malarial disease; also yellow fever and dysentery, though these are, perhaps, contagious also.

Diseases both miasmatic and contagious are anthrax, probably typhoid fever; possibly plague and cholera.

Ague, Intermittent Fever, Malaria.—There is no doubt that the poison of ague is contained in the soil of certain places, that it passes into the air and is absorbed by the breath. There is reason to think that it is also sometimes taken into the body with drinking-water.

The general name of malaria, or malarious poison, is given to the influence producing this disease: and the same influence is credited with producing other more severe forms of disease called remittent fever, pernicious malarial fever, malarial cachexia, etc.

It may be a question whether all these forms of fever are due to the same cause; but the general opinion is that they all constitute the same disease in various degrees of malignity. The one feature common to all is fever which remits and returns periodically. The other symptoms need not be considered here.

The malarial poison is found over a large part of the earth's surface, both in hot and in temperate climates. Certain conditions of moisture and vegetation greatly encourage its production, but cannot be said actually to produce it, since the same amount of moisture and of vegetation may be found in places where malaria is unknown. For instance, in northern countries, marshes and soils loaded with stagnant water are the seats of malaria: but the Roman Campagna, which is very dry, is notoriously infected with it. The exemption of the continent of Australia has been explained by the general dryness of the soil; but Tasmania, where the climate is humid and vegetation luxuriant, is still more completely exempt. Lowlands are doubtless more favorable to malaria than high stations, but it is known at great elevations, for instance, on the tableland of Castile in Spain, and on the eastern slopes of the Andes at an elevation of several thousand feet.

No kind of soil or geological formation has exclusively the power of fostering malaria, but some are more favorable to it than others. According to Parkes, the following are most so: 1. Alluvial soils, old estuaries, deltas. 2. Sands, if there is an impermeable clay or marly subsoil. 3. The lower parts of the chalk, where there is a subsoil of gault or clay. 4. Weathered granitic or trap rocks, if intermixed with vegetable matter. 5. Rich vegetable soils at the foot of hills (for instance, the jungle, or terai, in India).

The influence of high annual temperature is seen only in producing more pernicious forms of malaria, as in tropical compared with temperate climates.

The influence of season is shown by the fact that some districts which can be visited with safety in winter are extremely pernicious in summer.

It is also a well-ascertained fact that cultivation is extremely unfavorable to malaria, and in most cases soon destroys the poison. Agues were almost universal in England two or three centuries ago, but since great tracts of country have been drained and cultivated, the disease has become almost extinct, except in certain districts.

On the other hand the breaking up of malarious soil by excavations, etc., is known to be a dangerous process, by setting free the poison. Lands once cultivated, which are allowed to relapse into a wild state, often become again very fertile in malaria.

Malaria is not only, as has been shown, *endemic*, but may sometimes become *epidemic*, and such an epidemic may spread over a wide area.

For instance, two such epidemics are recorded in the history of our own country. One in the years 1678–9, which was so severe as to be called the "the new fever": another in 1718–22. Both these were generally spread over Europe. Such are often observed in countries where malaria is prevalent.

If we take a wide view of all these facts, it will be seen that they are just such generalizations as might be made about the distribution of species of animals and plants. A botanist may say that such and such soils in certain climates are suitable for the growth of certain plants, but it by no means follows that these species will be found there, even though the suitability of the soil may be shown by the rapid growth of the species if introduced.

The same analogy holds with regard to the extirpation of malaria by drainage and cultivation of the soil; for it is notorious that cultivation eradicates and destroys numerous species of plants and animals without any special effort on the part of the cultivator, merely because the physical conditions of the soil are no longer suitable for their existence.

Again, the relapse of such soils into an uncultivated condition is often followed by the re-appearance of some of these wild species.

We should hence conclude that it is highly probable that malarial poison depends upon some organism. animal or vegetable, which is either itself the poison, or generates the poison.

There are, in fact, only two other hypotheses possible. One is that some actual gaseous emanation from the soil is the cause. Sulphuretted hydrogen, marsh gas, etc., which are sometimes found in the air of malarious places, especially marshes, have been suggested. But it is quite certain that no inorganic poison can produce the symptoms of ague, since fever is, as we know, not produced by such an agent.

Moreover, since the poisoning is something which an infected person can carry away with him and preserve in his body for years, it cannot be a mere dose of some divisible substance, but must be something having the power of growth. Since, however, persons sometimes suffer in malarious places from transitory symptoms like those of poisoning, without acquiring any actual disease, it is possible there may be a volatile malarious poison, as well as an organism which produces it.

The only other hypothesis is that ague is a sort of permanent liability to chill, induced by the dampness or rapid changes of temperature said to be characteristic of malarious spots. But the changes of temperature which produce chills, etc., are characters of climate, not of malaria; and may be most conspicuous and extreme, without causing the disease. The climate of England has not materially changed within two centuries, and every winter thousands of persons are exposed to the most severe chills. Nevertheless, though they may acquire catarrhs and rheumatism, they do not, in these days, acquire ague. Again, persons may pass through a malarious place without suffering a chill or receiving any symptoms whatever; and yet may have carried away with them the ague-poison.

We conclude, then, that the hypothesis of a specific infective organism, having the power of living in the soil and also in the human body and of there producing fever, etc., is adequate to explain the facts of ague. Further, that no other hypothesis yet proposed is adequate to explain them.

Hence, according to the laws of scientific proof, if the assumed cause, the organism, could be proved to exist, the hypothesis would be scientifically demonstrated.

The one point in which this poison appears to differ from those of the other specific diseases is not being transmissible from man to man, no well-established instances of contagion being recorded. It has, however, lately been shown, (by Marchiafava and Celli) that the inoculation of the blood of an ague patient into healthy persons will reproduce the disease in them. The only possible source of fallacy here is, that the persons experimented upon may have been living in a malarious district and thus acquired the disease accidentally. But if so obvious a source of error was guarded against, the experiment clearly proves a multiplication of the poison, as in other specific diseases.

With regard to the nature of the poison, certain researches seemed to identify it with a certain bacillus found in the soil of malarious districts; but more recently an animal organism, a flagellate infusorium, has been found in the blood of ague-patients, which seems more probably the cause of the disease.

This will be described in the section on parasites.

Morbid Anatomy of Ague.—A patient affected with ordinary ague so rarely dies from it that nothing definite can be said about the post-mortem appearances, but in chronic cases, or sometimes in death from pernicious malarial fevers, characteristic appearances are met with.

The most marked change is the deposit in the tissues of the pigment, mostly dark brown or black, sometimes orange-colored, in the form of granules, sometimes contained in cells. This is seen in the spleen, liver, cortex of the brain, spinal cord, kidneys, heart, lungs, lymph-glands, skin, serous membrane, etc., as well as in the blood. The pigment is seen especially in the walls of bloodvessels, and is doubtless derived from the destruction of red blood-disks and setting free their hæmoglobin, which is broken up and forms the pigment. This appears to be taken up by the leucocytes and conveyed into the tissues by cell-migration.

Pigment-granules are also seen in the blood during life, in both classes of corpuscles and also free. There is evidence of great destruction of red blood-disks. In twenty-four hours an ague patient was found by Kelsch to lose one million blood-disks per millimetre cube (*see* Chapter XXVI. p. 271).

Besides these blood-changes, there is remarkable enlargement of the spleen, and in a less degree of the liver. In a case recorded by Dr. Maclean these two organs made up one-quarter of the total body-weight of a boy, the spleen weighing 10 lb. 15 oz., the liver 9 lb. 10 oz.

There are no other characteristic appearances. The material poison produces less distinct necrotic and degenerative changes in the tissues than are seen in the continued fevers, and does not cause acute local inflammation.

Certain special appearances in the blood will be spoken of afterward.

YELLOW FEVER.

The virus of this disease is chiefly miasmatic, existing and probably multiplying, outside the body. It thus exists, however, only in inhabited, and usually in thickly inhabited, places, so that something passing from human bodies appears to be concerned in keeping up the miasmatic poison.

The disease is endemic only in hot countries, and there is limited to commercial seaports and cities in communication with them by navigable rivers, and is almost confined to the American continent and islands. It has occasionally spread as an epidemic to European maritime cities, even to British ports, as Liverpool and Cardiff, and in southern Europe has spread widely over the country. In such cases the poison is conveyed undoubtedly by ships, and appears to pertain to the ship itself, rather than individuals.

There has been much controversy as to the actual seat or home of the poison, whether in the soil, in harbor mud, or bilge-water of certain ships. Into this question we cannot enter; it is enough that there is a material poison; that it is carried about in the way described; and that at one time or another it may be present in all these three situations.

But, on the other hand, there is some evidence that the virus, once established in the human body, may be given off to other bodies; that is, the disease is, in the ordinary sense, contagious. This is, however, not universally accepted.

There is no typical period of incubation for yellow fever; it may vary from one day to weeks or even months.

The virus introduced into the body causes fever and great degeneration of tissues, and especially of the blood, which shows signs of imperfect coagulation, dissolution of blood-corpuscles, etc., and putrefies very rapidly.

The liver after death is found greatly disorganized and jaundiced; the muscular substance of the heart remarkably degenerated.

The precise nature of the virus in yellow fever has not yet been determined, but it is evidently closely connected with or bred in decomposing animal matter, such as the mud of certain harbors and the bilge-water of ships. There is, however, in addition, a specific or human element, of which nothing certain can be said.

Partially Miasmatic Diseases.—Dysentery has been already spoken of as an infective disease, sometimes communicable. There can be no doubt that it is also a miasmatic disease, and that the poison exists in the soil of many parts of the world, especially in hot countries.

Typhoid fever may be, under certain circumstances, regarded as a miasmatic disease, since the poison exists in the soil or in water, and may be received thence into the body.

The same remark applies to cholera, and there are probably other local fevers, the species of which are not yet clearly distinguished, which also have their habitat in the soil or water of particular places, though they may be more widely distributed by human agency.

SIXTH CLASS OF SPECIFIC DISEASES; MYCOSES.

The affections of the skin and mucous surfaces produced by vegetable parasites are undoubtedly specific diseases, since they have a definite living virus or contagium, capable of conveying the disease. They differ from other specific diseases in retaining an exclusively local character. The living parasite, or, as it is called, *epiphyte*, produces a local affection of the part where it grows, called a *mycosis*.

or fungus-disease, but does not, with rare exceptions, enter the circulation so as to set up new foci of disease in internal parts, nor does it generate any toxic substance which is absorbed into the blood so as to cause general or functional disturbances. Hence these diseases—Ringworm, Thrush, and the like—are not *infective*, though they are *contagious* maladies.

The only known exceptions to this general law are as follows:

The spores of three species of a common form of mould fungus, Aspergillus, if injected into the blood of rabbits, have been found to grow in some of the internal organs, especially kidneys, liver, and muscles, so as to form colonies of the fungus. Death resulted if the quantity introduced was large. Moreover, the same fungus, one species of which has been seen as an ordinary epiphyte in the human ear, and has been found in human sputa, not infrequently establishes itself on the surface of the air-passages of birds, and has been known, when inhaled more deeply, to set up inflammation of the lungs, or pneumonia. Pneumonia from the same cause has also been sometimes observed in the lungs of cattle.

Another exceptional case of internal fungus-disease in man is that produced by the rare and remarkable vegetable parasite known as actinomyces. The commonest situation for this parasite is on the jaws of cattle, where it forms a whitish tumor-like mass, which works into the bone and causes necrosis. Passing further in, it may cause tumors, accompanied by suppuration, in the lymph-glands, lungs, and other parts. In man the same fungus has been found, though very rarely, in the crypts of the tonsils and also in internal organs, producing abscesses in the connective tissue and in the liver, pleurisy, peritonitis, and other affections, of which abscess of the liver appears to be, at all events in this country, the least rare. The botanical position of this organism, which will be described later on, is still uncertain. This and the other instances quoted show that it is not impossible for fungi of the same class as those which produce the common contagious skin-affections, to give rise to disease of internal organs.

In such cases, the history of the infection is analogous to that of the infective granulomata. There is an initial lesion at the point where the organism enters the body and secondary lesions of other parts, just as in the case of tubercle, syphilis, glanders, and the like.

CHAPTER XL.

PARASITES AND PARASITISM.

By a parasite is meant an organism which obtains its food and lodging at the expense of another organism, either in it or upon it.

Parasites may be either animal or vegetable, and may be parasitic either in or upon animals or plants. The parasites of plants do not concern us here, and we have only to consider the parasitic animals or plants of the human body. But it will be well first to take a cursory view of the laws of parasitism in general.

Parasitic organisms do not form a distinct division either of the animal or the vegetable kingdom, but they may be said to be, in general, low forms of life; feebler and lower in organization than the animal which bears them, which is called their "host."

Nor is parasitic existence distinguished by any absolutely clear line from existence in a free state. It is a matter of degree. Some organisms capable of a free existence are occasionally parasitic, some are constantly parasitic for a portion, at least, of their lives; some (though a smaller number) pass the whole of their life within the body of their host.

Hence we distinguish between *occasional parasites* or casual visitants, and *regular parasites*, which are so either through their whole life or for a certain period.

The distinction in the case of animals is obvious, and there is doubtless the same distinction to be drawn in the case of plants, though our knowledge of the life-history of the latter is not yet so complete.

In the animal forms certain broad differences of structure may be traced between the occasional and the regular parasites. The former must, for obvious reasons, be provided with organs of locomotion to convey them from one habitat to another, while in the latter class organs of locomotion are either wanting or imperfectly developed, since they are, as a rule, *sessile*. They are hence, speaking broadly, less highly organized than the former class. In compensation for this want, the sessile parasites are generally furnished with organs of prehension.

Comparison of Parasites with Free-living Animals.—It was at one time thought, and the notion was a very natural one, that parasitic animals belonged to species also found in the outside world; that intestinal worms or entozoa, for instance, were merely worms of the water or earth which lived in the human body. But careful observation soon showed that the species were different, and that intestinal entozoa were as incapable of living an independent life outside as an air-breathing annelid of living in the human bowels.

Nevertheless, certain affinities may be traced between certain parasites and certain external forms—for instance, between parasites of the alimentary canal, introduced with food, and other species of worms living in the water or among the herbage constituting the food of the higher animals which lodge the parasite.

If the parasitic animals be compared with those which are their nearest allies, it will be seen that, with a considerable amount of resemblance, there are certain general differences which serve to show that the animals are adapted for a parasitic life. These differences constitute the general law of parasitism from a natural history point of view, and are well worth consideration.

Parasitism involves a certain inferiority of organization, which, if the non-parasitic forms be regarded as the original or early types, must be regarded as a degeneration.

This degeneration is especially seen in certain systems; first of all, in the *digestive system*.

Parasites naturally do not require organs for seizing and dividing their food, which is supplied to them without any effort on their part, in a minutely divided or dissolved form.

Some of them have suctorial organs, but even these are wanting in many internal parasites. Tapeworms, for instance, absorb their food by endosmosis through the body-wall without any mouth at all.

Further, the organs for digestion and assimilation of food are very simple or wholly absent. Many intestinal worms have a simple straight intestine, but in the tapeworms even this is wanting. They are apparently able to apply the peptones and already digested foods of the alimentary canal to their nutrition without any further digestion.

In some parasites an equally marked simplification is seen in the respiratory system, if compared to that of the higher air-breathing forms to which they are allied. The Acarus scabiei, or itch-mite, for instance, though an air-breathing animal, absorbs the oxygen it requires by the general surface of its body, without any of the respiratory channels which in other arachnida are very well developed. This may seem an exceptional case. Nevertheless, the allied Acarus folliculorum is a still more remarkable instance of all the degenerations characteristic of parasitism. Its feet are short and out of proportion to the length of its body. Its general shape is wormlike; it has no organs of respiration, and those of digestion are extremely simple. If compared with an active, free-living mite or spider, it is evidently an animal of a much lower type.

The locomotive system is also very imperfectly developed in internal parasites. They are borne into or out of the body of their hosts mechanically, and when in the body are mostly sessile. If they are transferred from one part of the body to another, it is, in most cases, by wriggling movements which do not require special organs.

The organs of special sense are also, for obvious reasons, often undeveloped or very ill-developed in parasites.

Similar Law of Vegetable Parasites.—We have been speaking here of parasitic animals, but it should be observed that the same conditions of parasitic life may be traced, to some extent, in vegetable parasites also. They are not only plants of very low organization, but more lowly organized than those free species which seem to be their nearest allies. The ringworm fungus has many points of resemblance to the aërial moulds, but has a remarkable simplicity of organization as compared to them. The parasitic bacteria are, with few exceptions, among the simplest forms of the genera to which they respectively belong; while the micrococci present a monotonous simplicity of organization, which constitutes the great difficulty of classifying and distinguishing species that are evidently different in their physiological properties.

Economical Advantages of a Parasitic Life.—From what has been said, it will be evident that parasites live in conditions extremely favorable to nutrition. They are kept at a constant and relatively high temperature, which is maintained without any consumption of their own material or food; they have regular supplies of food, for the most part already digested, in the form of peptones, which can be assimilated with little waste. Not exercising to any degree locomotion or other active function, they consume no material and waste no energy. Consequently nearly the whole of their abundant food is applied to nutrition, and there being so little functional waste, nearly all goes to growth. Hence the growth of some internal parasites is fabulously rapid (if the production of eggs be taken to be what it really is, a kind of growth), and the living material of their bodies is probably increased and multiplied in a higher ratio in a given time than is the case with any other animals.

Metamorphoses of Parasites.—Many parasites belong to those classes of animals which undergo marked changes of form before arriving at maturity. These are either transformations, such as those of insects, in which the individual passes through several stages before attaining sexual maturity, or else the more complex process called "alternation of generations," which consists in an alternation of two modes of reproduction—that by gemmation or budding, which produces a "colony" of more or less imperfect individuals; and that by sexual union, producing eggs. These processes involve interesting zoölogical questions, but are only important here in so far that parasites which pass through such transformations as these are suited, in their different stages, for parasitic or for free life respectively; the change from one form to the other being coincident with a change in the habitat of the parasite.

No typical parasite goes through its whole life-history in one place. Supposing it to start with a free life outside the body in one stage of development, it then begins another stage when it enters the body of its host. After passing through this stage as a parasite, it then returns to free life again, thus completing the circle. In many cases the parasitic life is divided into two stages, which may be gone through in two different hosts, or, less commonly, in two parts of the same host. When two animals lodge the parasite successively, that which lodges the imperfect or larval form is called the "intermediate host." The parasite does not live on in the same stage of its existence in the two hosts, but in one it is an imperfect or juvenile form, in the other in the mature form.

Thus the two stages of development of a tapeworm, the cystic and cestoid forms, are gone through in two distinct hosts. It is possible, though not common, for two individuals of the same species to act as the two hosts successively of a parasite. This is the case with trichina spiralis.

Limitation of Parasites to Certain Species.—Parasites cannot live indifferently in various species of animals, even though the conditions may seem to be the same or similar in all. Some are confined to one host. This is apparently the case among human parasites with *Bothriocephalus latus*, or the broad tapeworm, *Oxyuris vermicularis*, the common threadworm, and with the head-louse, which species are not known to occur in or on any other animals. Probably this is true of others also.

In some cases the parasite infests allied species, as the little tapeworm (*Tænia echinococcus*), peculiar to the dog and wolf, and the *Tænia mediocanellata*, which in its cystic state is found in various kinds of horned cattle, while the allied species, *Tænia solium*, affects the pig.

There are some parasitic species of which the range is much wider. Thus the common fluke of sheep (*Distoma hepaticum*) is found, not only in that species, but in most ruminants, in pachyderms, in horses and in rodents, as well as, rarely, in man. The trichina spiralis is still more universal in its distribution, being found not only in its most frequent host, the pig, but in various herbivorous animals, as the rabbit, ox, and horse; also in carnivora—the fox, dog, cat; and even —what is rare for a mammalian parasite—in birds.

This degree of indifference, is, however, rare; generally the range of parasites is limited by certain laws, to which there are few exceptions; so that the case of a parasite "going wrong" and getting into another than its regular host, seldom happens.

The chief law which regulates this distribution is that of food. Many parasites enter the body of their hosts with food or water, and hence can only infect those which live on a similar diet. But even among these many possess an immunity against certain parasites. Horses, for instance, do not usually get the same as cattle, though feeding on the same land.

Other species have acquired the habit of fixing themselves in such a part of one animal as serves for food to another, for instance, the muscles and the liver. Hence, such will be found in their next phase of existence only in carnivorous animals. Speaking broadly, the parasites of flesh-eaters and grass-feeders can be distinguished. Man, through his omnivorous diet, is liable to be infested by both classes.

In consequence of these food-relations many parasites are entirely dependent for their existence upon the mutual relations of two higher animals, for instance, man and some other. If man did not keep about him domestic animals, use some of them for food, and share with some the same water and the same food, the life-history of tape-worms could not be completed.

The adaptation of parasites to the conditions of life of their host is astonishing. Take one instance from another than a human parasite. There is a little worm belonging to the genus Mermis, which is often found in immense numbers on moist earth, especially after rain so as to give rise to the story of worms falling with the rain from the sky. The sudden abundance of the little worms has, however, been shown to be due to their having escaped from the bodies of winged insects (flies or moth) in which they were parasitic; and the object of their escape is to deposit their eggs in the ground.

In the ground the eggs rest during the winter along with the eggs of their insect host. In the spring both broods are simultaneously hatched; and the embryos of mermis at once proceed to penetrate the bodies of the young insect larvæ which are hatched at the same time. The parasite remains in the body of the insect through all the transformations of the latter, till at length, in the perfect insect or imago, the little mermis is carried about to some damp situation which the insect chooses for laying its eggs, and where the worm also finds a suitable nidus.

Another worm, Gordius, which lives in water, penetrates aquatic insect larvæ in the same way, and the embryos of both worms have been seen to penetrate the larvæ of moths and ephemeræ respectively with which they were experimentally brought in contact.

The importance of these instincts in the life-history of the parasites is as follows. The shallow pools or marshy places which are their natural habitat are very liable to dry up, and in this case the worms would die, or their embryos would be unable to develop. But, taking advantage of the instincts and superior powers of locomotion of winged insects, they get themselves transported to other pools or damp places.

To enlarge upon this subject would be out of place here; but the life-history of most parasites shows that the parasitic habit would give the species an advantage over other allied non-parasitic species, and thus, on Darwin's principles, would account for the origin of parasitic species.

The history of the Filaria sanguinis hominis, as told by Manson, is a no less remarkable instance of adaptation. This little worm appears to pass, by means of drinking-water, into the human intestine. Its embryos, by means to be afterward described, emigrate thence into the lymphatics and into the blood, which contains incredible numbers of them.

If the little creature had no means of getting out of the blood into the water where its parent lived, and where it can complete its development, the species would come to an end. But an intermediate carrier-host is supplied, in the shape of the blood-sucking mosquito, which, as is well known, visits the human skin mostly in the evening. During the daytime the blood of the person affected with filariæ contains few embryos, but as evening approaches, the blood swarms with them, escaped, it would seem, from the lymphatics, where they harbor during the day. So numerous are they that the tiny drop of blood drawn by the blood-sucker must contain some of them. When the female mosquito (for pregnant females are the chief, if not only, blood-suckers) has finished her meal she retires to the surface of the water, where instinct prompts her to lay her eggs. Having done so, like some other insects in the same circumstances, she dies, and the embryonic filariæ are, by decomposition, set free in the element whence their parents came. Here we see that the blood-parasite adapts itself, not only to the conditions of its human host, but to the nocturnal habits of the intermediate host, itself an occasional parasite of man.

Part of the Body Affected by Parasites.—The distribution of parasites in the body is not a matter of indifference. Some, as has been said (known as *Ectozoa*), live on the skin, and often in special parts of it only; some being confined to the hair of the head, some to the short hairs on the pubes or other parts of the body. Internal parasites or *entozoa* show considerable variety in their distribution. Many species can only live in the intestinal canal, and affect generally one part of it rather than another. There are others belonging to the blood and lymph. Those which live in solid organs have a more varied distribution, as hydatids, which, though generally found in the liver, are found in other situations also. Those which belong to muscle and connective tissue, such as cystic parasites, have a considerably wider range, as will appear in describing the different species.

In the case of those parasites which go through several changes of form, it very generally happens that each form has its habitat in some particular tissue; *e. g.*, tape-worms in the intestine, their cystic forms in the tissues, and for the most part when changing their host they pass into another phase of existence and also into a different part of the body.

Less commonly, parasites, in changing their form, pass from one part to another of the body of the same individual.

Productiveness of Parasites.—The reproduction of these animals nearly always takes place during their parasitic life. Even those which pass a portion of their life in a free state rarely or never produce ova in that condition.

In fact, the conditions of parasitic life, where food is very abundant and early assimilated, are very favorable to reproduction, and hence we find that the fertility of parasites is very great indeed. The entozoa produce enormous numbers of eggs. For instance, one ripe joint of Tænia solium is estimated to contain 53,000 eggs, and if we suppose that only 800 such joints are cast off in a year (though sometimes two or three are passed daily) the annual produce in eggs will be some 42,000,000. The round-worm (Ascaris lumbricoides) is estimated to produce in the year some 64,000,000 eggs. The gigantic productiveness of these creatures is even better shown if we consider the actual mass of material thus produced. Though the egg of an ascaris is extremely minute, its diameter being represented by a twentieth of a millimetre, the total weight of the yearly produce of eggs comes, according to Leuckart, to a mass 1740 times that of the parent worm. This is a much higher fertility even than that of the queen bee, which produces 130 times her own weight in the form of eggs.

If we compare it with the case of our own species we find that it is a high degree of fertility for a woman to produce one child yearly for some years. This represents a production which may be at seven per cent. of the body-weight; so that, to equal the fertility of the ascaris, the human female would have to produce about 25,000 children in the year, or, say, seventy daily.

This fabulous prodigality of reproduction would seem to involve enormous waste; but really the number of eggs does not appear to be more than enough to continue the species, since the numbers of parasites do not apparently increase. The chances against any egg reaching the body of another animal where it can develop, must therefore be some millions to one.

The sexually mature state in which eggs are produced is often, as has been said, only one stage in the life of a parasite, but this stage is always gone through in the body of its host, where food is abundant, not in a free state. The eggs are, on the other hand, generally developed outside, and there is perhaps no instance known of the eggs of a true parasite being hatched, and the embryos growing up in the same place as the parents. At all events, according to Leuckart, no truly parasitic intestinal worm goes through the whole of its life-history in one place.

Changes Produced by Parasites in the Organism.—The consequences arising from the presence of parasites in the body of the host are extremely various, depending in each case upon the nature of the parasite itself and its situation.

Death is naturally an infrequent result, since it would, in most cases, be opposed to the law of self-preservation on the part of the parasite, that it should kill its host. This will never happen unless the death of the host is a necessary link in the life-history of the parasite, as is the case, for instance, with the common liver-flukes of sheep. These parasites are fatal to sheep; and the carcasses, if allowed, as they would be under natural circumstances, to lie and putrefy on the pastures, permit the escape of the flukes into the grass or water where they have to undergo their further transformations.

There is only one result which is quite general, and applies to all parasites without exception, though in very varying degrees of importance: that is, the withdrawal of a certain amount of nourishment; and since the parasite never becomes food for his host, this amount is permanently lost. The loss from this cause is, however, generally inconsiderable; and it is only in the case of comparatively large intestinal worms that it can be regarded as capable of estimation. In the tapeworm, for instance, a certain amount of material is continually being thrown off in the shape of ripe joints, all of which have been formed at the expense of the human body.

That blood parasites, such as those mentioned above, also produce some general constitutional disturbance need hardly be said, but with these exceptions the symptoms produced by animal parasites are local.

These local or organic disturbances may be comprised under the three heads of—Destruction, Pressure, and Irritation.

Material Loss Caused by Parasites.—It is calculated by Leuckart that the broad tape-worm (Bothriocephalus) discharges in the course of a year about 140 gm. or 4½ ounces of ripe joints. Some chemical change or metabolism is necessary to the formation of tissues; this would involve a waste of three or four times that amount, say one pound—an amount obviously insignificant. The common beef tape-worm, he calculates, may give off in the year about one pound of material in the same form, involving a total consumption of three or four pounds, also an inconsiderable quantity. The ascaris, or round-worm, brings forth, according to the same authority, an annual produce of eggs which represents a loss of about three ounces—a very small amount; but if there should be many of them (suppose one hundred, though this is a very rare occurrence) then the above amount multiplied by one hundred would give 20 pounds annually, or nearly 2 pounds a month; a loss which, for a child, would not be inconsiderable.

There is another intestinal parasite which, though insignificant in itself, occurs in such enormous numbers that its growth and multiplication withdraw a notable amount of material from the body—the *Rhabdolitis stercoralis*, which is the cause of the disease called Cochin China diarrhœa, and of which one hundred thousand may be discharged daily from the bowels. The actual weight of these, minute as they are, is calculated to be about six ounces, involving a loss of nutriment to the patient of more than one pound daily, from which, combined with the exhaustion produced by the accompanying diarrhœa, rapid emaciation and cachexia result.

A still more evident cause of cachexia is the loss of blood caused by some internal parasites. Among these is chiefly to be noticed the Ankylostoma (Dochmius) duodenale, a worm which lives in the small intestine and sucks blood like a leech. The malady produced by this, and by the accompanying intestinal inflammation, is so serious as to have been recognized as a distinct form of anæmia (Egyptian chlorosis), which is sometimes fatal.

Other blood parasites, the Filaria sanguinis hominis, and the Bilharzia (Distoma) hæmatobia, also cause hemorrhage and anæmia.

Speaking generally, these grave disturbances of nutrition, as a consequence of parasitic life, are rare, and there are only a few instances in which any other general disturbance, such as *fever*, is produced.

The latter symptom, however, in a very marked form results from the passage to the muscles and other parts, of immense numbers of the embryonic Trichina spiralis, so that the resulting disease, serious and sometimes fatal, has received the name of Trichiniasis. The special symptoms occur when the parasites leave the bowel.

Local Lesions Produced by Parasites.—Although the popular conception of an internal parasite represents it as eating up the vitals of its victim, actual destruction of any organ is not common. The most conspicuous instance is one outside human pathology, in the common liver-fluke (Distoma) of the sheep—a rare visitor in man—which destroys the organ in which it takes up its abode, so that it appears after death almost liquefied, and great numbers of sheep die from this cause.

Intestinal worms occasionally perforate the coats of the intestine and pass into the peritoneum and other parts. Hydatid cysts of the liver sometimes cause destructive suppuration of the organ.

For the most part the effect on the organs is merely that of passive pressure, such as would be caused by any other foreign body or tumor. Should the organ be one as delicate as the brain or the eye, it is clear that, even from this, very serious consequences may result. Large hydatid cysts of the liver may also by their size produce serious results.

When a parasite becomes imbedded in the tissues, the organism treats it as a foreign body, surrounds it with a capsule, or, under certain circumstances, sets up suppuration, which may have the effect of causing its expulsion. But when once surrounded by a capsule, many kinds—for instance, the cystic parasites—may remain quiescent for years, or even till they are set free by the death of their host.

Mechanical irritation, on the other hand, is caused by parasites which have some power of movement, such as entozoa, in the alimentary canal; or still more by those which pass from one organ to another. Reflex disturbances of the nervous system are often thus set up, which will be noticed in speaking of the different species.

CHAPTER XLI.

ANIMAL PARASITES.

THESE belong to the sub-kingdoms, Protozoa, Vermes and Arthropoda.

PROTOZOA.

The simplest known forms of animal parasites belong to the class *Rhizopoda* and genus *Amœba*. These are minute animals with a body composed of granular protoplasm containing a nucleus and contractile vesicles. Their form is very variable, but may be considered spherical when at rest. Like the other Rhizopoda, they put out protoplasmic processes known as Pseudopodia, and this is one means by which their change of form is effected. They absorb their food by surrounding and enclosing it, when it is digested within their body and the undigested residue expelled. They multiply by simple division.

These simple creatures have one point of interest in respect to histology and pathology, since it is from analogy with them that the name "amœboid" is given to leucocytes or mobile cells of higher animals. These elements, as has been already pointed out, alter their form, move about and absorb foreign bodies much in the same way as the free-living amœbæ.

Amœbæ are common parasites in some of the lower animals, such as insects, and are occasionally found in higher animals.

One species only has been observed in man, called *Amœba coli*, and this was only once seen (by Lösch) in large numbers, associated with a dysenteric affection of the colon. It has also been seen in cases of dysentery in Egypt.

Its size is from 0.02 to 0.035 mm., that is, 2½ to 4 times the diameter of a red blood-disk.

Whether these creatures have any pathological importance cannot be said.

Another form belongs to the family Gregarinidæ and genus *Co dium.* They are of roundish or oval shape, and consist of protoplasm with a condensed outer layer, without any organs properly so-called. Spores are formed in the interior. They are found encapsuled in the internal organs of several species of animals, especially rabbits, and have very rarely been found in the human subject, in the intestines and liver; and in this form have been called Psorosperms.

Coccidium oviforme, found rarely in the human liver, is about 0.033 mm. long by 0.015 or 0.02 broad. According to Leuckart, it lives when young within epithelial cells, and afterward forms a capsule. They are, apparently, of no pathological importance in man, but are destructive to rabbits. Singular oval bodies, discovered by Mr. Rainey in the muscles of pigs, and called Rainey's capsules, are thought to be of the same nature.

Recently Bollinger has put forward the hypothesis that certain peculiar bodies, somewhat smaller than an epidermic cell, found in the disease called *molluscum contagiosum*, which forms little tumors of the skin, are gregarines; but this is not proved. I have never seen any movement or other sign of life in these bodies.

The identification of certain minute masses found on the hairs, in some countries, with gregarines, is still more uncertain.

Infusoria, a higher group of Protozoa, occur in the human body in certain cases.

The family Monadina have a simple transparent body with one or more delicate filaments or *flagella*. Many species live free in water; many are parasitic in various animals.

Cercomonas Intestinalis is an oval infusorian, about $\frac{1}{2500}$ of an inch in length, with one end tapering and pointed, the other broad and round, with a long flagellum.

It is found in the intestine in chronic diarrhœa; sometimes in dysentery and typhoid fever. It is said to be especially abundant in the mucous covering of the small intestine in children with diarrhœa. Though more abundant the more profuse the diarrhœa, there is reason to think that this is only because the mucous secretion forms a suitable habitat for the animalcule, and that it is not a cause of disease.

Cercomonas Urinarius was found by Hassall in alkaline urine.

Trichomonas Vaginalis is found in the mucus of the vagina, especially in catarrhal conditions, but has probably nothing to do with causing the inflammation.

It is larger than the last mentioned species, being about $\frac{1}{1600}$ of an inch in length, with flagella one to three in number, and also some minute hair-like processes which resemble cilia.

A true ciliated infusorian, the Paramœcium coli (or Balantidium), has been found in the colon, sometimes in very large numbers.

It occurs also in the intestines of swine, but appears to be local in its distribution, having been more often found in Sweden than in any other country.

Flagellated Infusoria in the Blood.—It has long been known that flagellate infusoria are occasionally found in the blood of frogs, and, more lately, minute animals have been discovered in the blood of rats, first by Lewis in India, afterward by Crookshank in London, which appear to belong to the class Infusoria, and much resemble the genus Trichomonas.

Those seen by Lewis were tapering animalcules about $\frac{1}{1200}$ to [illegible] of an inch in length, furnished with a long lash-like thread or flagellum as long as the body itself at one end. They were found in healthy animals. Wittich found similar organisms in the blood of the hamster (*Cricetus vulgaris*), an observation confirmed by Koch. Flagellated organisms apparently similar have been found in the blood of certain fish, viz., the mudfish and the German carp. In none of these cases did the infusorian appear to give rise to any morbid symptoms.

In a fatal disease of horses, mules, and camels in India known as "surra," the blood of the affected animals was found by Evans to contain large numbers of a similar parasite, which appeared during the febrile period of the disease, and was wanting when the fever subsided.

Crookshank has lately investigated the parasite of surra, and finds "the somewhat tapering central portion or body of the parasite to be continuous at one end with a whip-like lash, and at the other end to terminate in an acutely pointed stiff filament or spinelike process."

He has also found an infusorian identical in form in the blood of about twenty-five per cent. of common brown rats, and regarding all these flagellated organisms as probably of the same species, suggests for it the name of *Trichomonas sanguinis*. Although the parasite of surra is apparently the cause of the disease, Crookshank remarks that this is not yet positively proved.[1]

Blood-parasites in Malaria.—A remarkable motile body has been observed in the blood of patients suffering from ague and other forms of malarial disease, which is certainly an animal parasite, and perhaps a flagellated infusorian, but more probably belongs to the class of *Mycetozoa* (or fungus-animalcules), which lie on the confines of animal and vegetable life. It was described some years ago by Laveran in Algiers, and though his observations attracted at first little attention, they have lately been confirmed by a number of observers—*e. g.*, Richard in France, Marchiafava and Celli, Golgi and others in Italy, Councilman, Sternberg, Osler and others in America. The organism in question has been called *Plasmodium malariæ* by Marchiafava and Celli, but Osler, who regards it, perhaps on inadequate grounds, as an infusorian, calls it *Hæmatomonas sanguinas*.

Laveran first observed within the red blood-corpuscles certain small granular or hyaline masses, usually containing pigment, and showing spontaneous changes of form. They vary in size from one-fourth to nearly the whole diameter of a blood-corpuscle. They are evidently amœboid organisms which absorb pigment from the corpuscles, so that the latter are often paler than usual, and are sometimes converted into colorless shells (Osler). They have never been observed to leave the corpuscles, and are only rarely observed in leucocytes. In some cases, pure hyaline masses containing no pigment have been seen, which some consider as an early stage of the pigmented bodies, others as something entirely different. But pigment is sometimes absent, even in very severe cases of malaria. These organisms, in certain cases, increase in size, till they become as large as the blood-corpuscles, from which they then escape and become free. After this, they undergo segmentation, and break up into a number of small, round bodies, which are either spores or young individuals, the process somewhat resembling spore-formation in the Gregarinidæ, and other Sporozoa. This development occupies, according to Golgi, a period of three days, corresponding to a quartan ague; but, in cases of tertian the process was more rapid.

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[1] See Crookshank, Manual of Bacteriology, second edition, page 350, for further reference.

Beside these intracellular forms, others are found free, which are believed to be stages in the development of the same species. One kind are the "crescents" of Laveran, pigmented crescent-shaped bodies, larger than blood-corpuscles, and thought to represent an encysted form, being sometimes found of a smaller size within the corpuscles. Another form is a free flagellated organism like an infusorian or monad. It is smaller than a blood-corpuscle, and furnished with one to four flagella, which are in active and rapid motion. The precise connection with the other forms has not yet been traced, but it is quite in accordance with analogy that this should be one of the stages of development of the parasite.

Small, free, pigmented bodies, like those within the corpuscles, are also sometimes seen.

Relations of the Parasite to Disease.—As to the relation of the numbers of these organisms to the paroxysms of ague, statements differ; but it would appear that they are more numerous the more severe the disease. The larger developmental forms which produce spores, or quasi-spores, are chiefly found during the paroxysms, and disappear in the intervening periods, but the intracellular bodies are constant. In cases treated with quinine all the parasites disappear entirely as the disease is cured. Every variety of malarial disease, acute and chronic, including pernicious malarial fever, shows the parasite.

It has been found in the kidney, spleen and liver of the fatal cases, and Councilman observed it in the capillaries of the brain in cases of fatal malarial fever, of which coma was a marked feature.

As to the question whether the parasite is the cause of the disease, it must be remarked first, that we have here a parasite, the presence of which in the blood-corpuscles explains some of the most marked features of malaria, viz., anæmia from destruction of blood-corpuscles and deposit of pigment in various organs (see page 391).

The periodicity of ague also, if Golgi is right, corresponds to the periodical development of the parasite. The constancy of occurrence of the organism in the blood of malarious patients, and its absence in that of persons healthy or otherwise diseased, is an important argument of coincidence, and is strengthened by the fact that quinine, in curing the disease, causes the parasite to disappear from the blood.

It has never been found possible to keep the organism alive apart from the body and test its morbific action by introducing it into the blood of another individual. But, as has been mentioned, the blood of ague patients containing these parasites has been found experimentally to convey ague to healthy persons.[1]

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[1] See Laveran, Traité des fièvres palustres, Paris, 1884; and for other references, Baumgarten's Jahresbericht über Mikroörganismen for 1885 and 1886; also Osler, Brit. Med. Journal, 1887, vol. i. p. 556.

VERMES.

The worms furnish a much more important group of parasites. They are what are generally known as entozoa.

Three orders include species which are parasitic in the human body, viz., Nematoda, Trematoda, Cestoda.

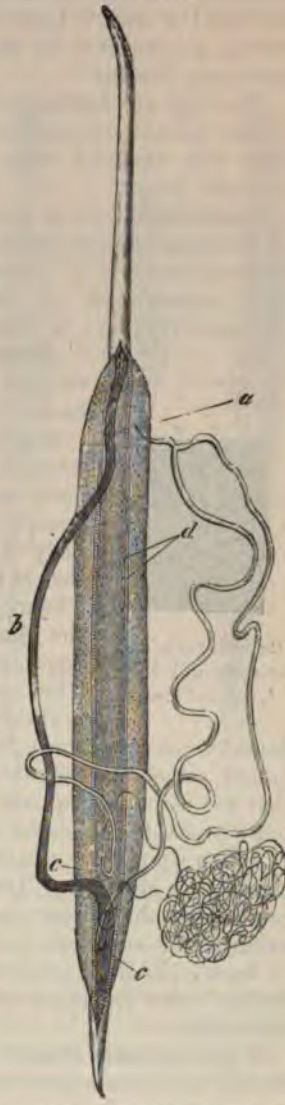
The Nematoda are a numerous group, some of which are parasitic in man or other animals, some lead an independent life.

The Nematode parasites which will be here described, are:

Ascaris lumbricoides; A. mystax; Oxyuris vermicularis; Trichocephalus dispar; Ankylostoma duodenale; Trichina spiralis; Filaria sanguinis hominis; Filaria medinensis.

All these worms are simple—that is, they do not form compound zooids or colonies; they undergo no transformations between the egg and the adult state; the sexes are distinct, and there is usually a marked disparity between the male and the female. They have distinct digestive organs, which, as well as the generative organs, are loosely suspended in a perivisceral cavity.

FIG. 86.



Ascaris lumbricoides, dissected. (HELLER.)

a, genital orifice; *b*, intestine; *c*, oviducts; *d*, longitudinal band; *e*, ovaries.

Ascaris Lumbricoides; Round-worm.—A smooth, flesh-colored or pale brown worm, which has its specific name from its likeness to the common earth-worm. Both ends taper, but especially the posterior. At the anterior extremity is a mouth with three papillæ. The female measures ten to fourteen inches long, and a quarter of an inch in thickness. The male is four to six inches long, and more slender than the female. The male has a curved tail furnished with a penis with two hooklets. The female has a genital orifice in the anterior half of the body. The ovaries are very complicated, consisting of two tortuous tubes, which, when unravelled, are each about four feet long, and contain enormous numbers of eggs. Sometimes only one worm occurs, sometimes two or three, rarely large numbers, up to some hundreds. Their proper habitat is the ileum, but they may migrate into the stomach, and thus to the mouth or nose; also into the colon and out through the anus. Less commonly they perforate the wall of the intestine, passing into the peritoneum or surrounding tissues, sometimes producing abscess.

The eggs are discharged in great numbers per anum. They require several months to come to maturity. They probably enter the human body with drinking water as small embryos, but their life-history is not fully known.

Symptoms.—The presence of one or a few round-worms produces no recognizable symptoms, and the diagnosis is generally made only on seeing the worm. When in large numbers they are said to cause colic, constipation or diarrhœa, vomiting, and also symptoms of nervous irritation; in children, even convulsions.

FIG. 87.

Oxyuris vermicularis (natural size). 1, female; 2, male.

Ascaris mystax, the small round-worm of the cat, has in a few cases been found in the human body (Cobbold).

Oxyuris vermicularis; **Thread-worm**.—Is somewhat like the Ascaris in shape, but very small, the male measuring one-sixth of an inch in length; the female, one-third or two-fifths of an inch. The body of the female tapers posteriorly to a point; that of the male is blunter and often bears a spine. The mouth has three papillæ. The arrangement of the genital organs is like that in Ascaris. The eggs are oblong, somewhat irregular in shape. They are discharged in great numbers, and are probably, in the case of children, sometimes accidentally conveyed away by the finger-nails, and reintroduced into the mouth, which explains the persistence of the parasite. It is supposed that the worm is acquired by eating uncooked fruit; but water is a more probable vehicle for its introduction into the human body.

These worms are usually present in very large numbers, and are common in children. Their habitat is the large intestine; and it is said chiefly the cæcum; but they often pass to the rectum, where they excite great irritation, and sometimes wander to the outside, and may, in female children, enter the vaginia. Itching is also felt in the nose; and by reflex irritation cough may be excited, as well as other nervous symptoms.

Trichocephalus Dispar.—This remarkable little worm is known by having the anterior two-thirds of its body much smaller than the rest, so as to form a delicate filiform neck, by which it is anchored in the mucus of the bowel. The male measures one and a half inches in length; the female two inches. The posterior, thicker part of the body in the male is curved, and has a penis with recurved spines at its extremity. This part of the body in the female is straight; the genital orifice is at the junction of the thicker and thinner parts. The eggs are $\frac{1}{480}$ to about $\frac{1}{440}$ of an inch in their longest diameter (Cobbold). They develop only out of the body, and very slowly, six months at least being required before the embryo is formed. The habitat is the cæcum coli, where the parasite is sometimes found in great numbers. It is seldom discharged per anum. Though said to be very common in Germany, this worm is certainly not often met with in this country. It appears to be quite innocuous.

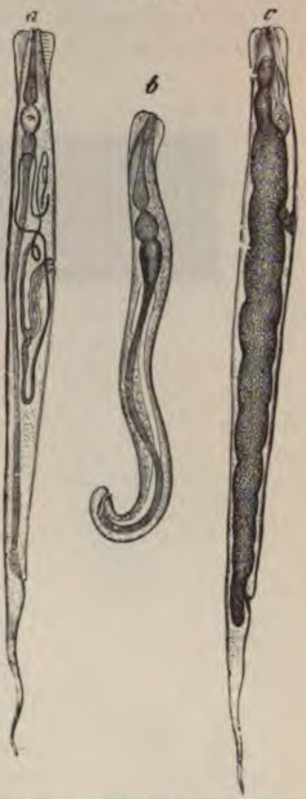
Ankylostoma Duodenale (Syn.: Dochmius duodenalis; Strongylus duod.; Sclerostoma duod.)—A round-worm about one-third of an inch long, the female somewhat more. The mouth has four unequal and unsymmetrical papillæ. The reproduction is viviparous according to Cobbold.

It lives in the duodenum, or beginning of jejunum, sometimes in very large numbers, and sucks blood from the small vessels. By this, and by subsequent hemorrhage from the bite, great anæmia is produced, constituting the disease known as Egyptian chlorosis.

The worm was first observed in North Italy, afterward in Egypt; and seems to occur also in some tropical countries, *e.g.*, Cayenne and Brazil. Of late years it has attracted attention as attacking workmen engaged in making the St. Gothard tunnel.

Trichina Spiralis.—*Description.* (Cobbold). A minute worm, the female measuring $\frac{1}{8}$ of an inch, the male about $\frac{1}{18}$ when mature; body, thread-like, usually somewhat bent upon itself, rather thicker behind than in front; head pointed, unarmed, with a simple central mouth. The male has a sort of tail, composed of two lobes, between which is the anus; the penis consists of a single **V**-shaped spicule. The female is stouter than the male, rounded posteriorly, the genital orifice near the head. The eggs measure $\frac{1}{1270}$ of an inch in their long diameter; the mode of reproduction is ovo-viviparous, the eggs being hatched within the body of the mother.

Fig. 88.



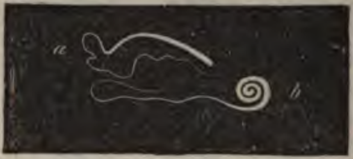
Oxyuris vermicularis (magnified). *a*, young female; *b*, male; *c*, mature female, full of eggs.

The adult form is found in the intestine of various animals including man.

The larvel form, much more often seen, is found in the muscles, and generally in immense numbers. It is a very small creature, about $\frac{1}{30}$ of an inch long, by $\frac{1}{600}$ to $\frac{1}{700}$ in diameter, with a digestive apparatus and imperfectly developed sexual organs. It is usually found coiled up, and sometimes enclosed in a capsule, sometimes not; the larval and mature forms are always found in these two situations respectively, and not *vice versa*, a fact most important to bear in mind.

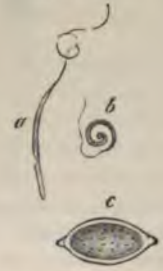
The larval form was discovered in human muscle by Sir James Paget (then a student) in 1835, and described by Professor Owen. It was afterward widely recognized, but its connection with the adult intestinal worm was not shown till twenty years later, by Leuckart.

FIG. 89.



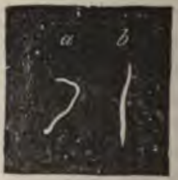
Trichocephalus dispar (natural size).
a, female: *b*, male.

FIG. 90.



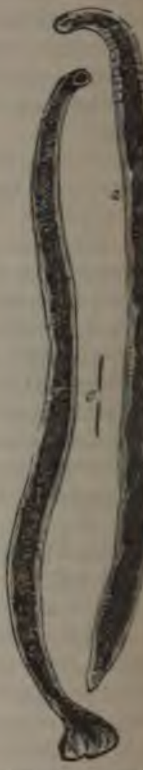
Trichocephalus dispar (BRISTOWE).
a, female ; *b*, male ;
c, egg (magnified).

FIG. 91.



Ankylostoma duodenale (natural size).
a, male ; *b*, female.

FIG. 92.



Ankylostoma duodenale (magnified, after BRISTOWE).
a, female ; *b*, male.

The life-history by which these forms are connected has been ascertained by very numerous experiments of feeding animals with trichinous flesh. Suppose a piece of muscle containing the larval trichinæ to come into the digestive organs of a dog, a pig, rat, or any other animal, to which it may be given experimentally. If killed two days afterward, the intestines will be found to contain full-grown and sexually mature worms. In an animal killed after six days, the female trichinæ are seen to enclose perfectly formed and free embryos in their interior. These pass out through the genital orifice, and immediately begin burrowing through the intestinal wall so as to get into the peritoneum, pericardium, and all surrounding tissues; but they do not permanently rest till they reach voluntary muscle. They may affect all muscles; the diaphragm, and muscles of the neck, pharynx, and larynx most abundantly, but the heart very rarely. They penetrate within the sarcolemma, cause degeneration of the fibre and surrounding inflammation.

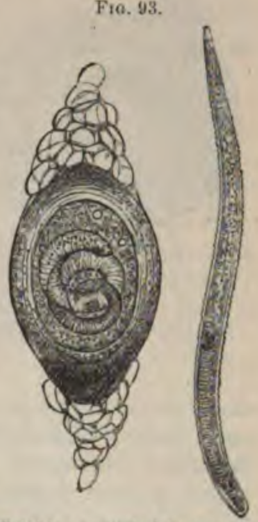
In about fourteen days they attain the full (larval) size, after this they become encapsulated, a process which occupies some months. The larval worm first becomes surrounded with a chitinous investment secreted by itself; afterward a wall of fibrous tissue is formed from the surrounding perimysium which often shows adipose tissue at each end.

The capsule undergoes calcareous infiltration, and a small hard chalky granule is produced, just visible to the naked eye, within which, if cleared up by acids, the coiled-up larvæ may be seen. In this condition the creature ceases to grow, but may remain in a living, though a quiescent, state for years; but many die. Before its encapsulation it is seen with difficulty.

Trichinæ in muscle are sometimes enormously numerous; one ounce of muscle has been calculated to contain more than 300,000, so that no less than 30,000,000 might be harbored in one individual. Sometimes they are few in number.

When set free from the capsule, after the death of their host either by putrefaction or digestion, the larvæ may live in water for a month or more. Hence, by putrefaction of a carcass, they may get into drinking water, and thus pass into the stomachs of herbivorous as well as carnivorous animals.

FIG. 93.



Trichina encysted in muscle and free (BRISTOWE).

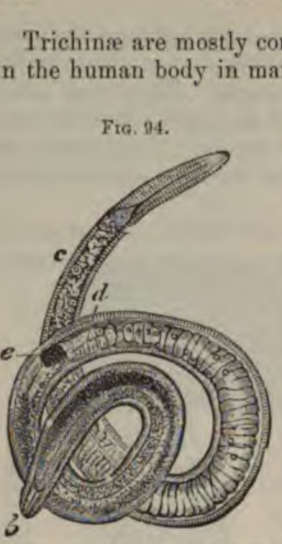
The full-grown intestinal trichinæ live only a few weeks, but in this time each female may have given birth to a thousand living embryos. They soon die after the death of their host.

While migrating through the tissues, the embryos produce no definite symptoms if few in number; but if very numerous, a febrile condition is set up which has much resemblance to typhoid fever, and has doubtless sometimes been mistaken for the disease. It may be fatal, and in Germany severe and destructive epidemics of *trichinosis* have been produced by eating uncooked pork or sausages derived from animals infected with trichinæ. Isolated cases occur in this country, but no such epidemic has been certainly proved to exist here; though groups of suspicious cases have been observed.

The diagnosis may sometimes be made by removing a small portion of muscle during life.

Trichinæ are mostly common in pigs, rats, and mice, and are found in the human body in many countries where the flesh of pigs is eaten imperfectly cooked. This is the chief and perhaps the only means by which they infect mankind.

FIG. 94.



Mature trichina spiralis, magnified (CORNIL and RANVIER).

c, head, with mouth and œsophagus; b, anus: e, genital organs.

Experimentally, it is found that most quadrupeds and even some birds, are susceptible of infection by eating trichinous flesh.

Filaria Sanguinis Hominis.—This extraordinary and interesting parasite occurs in tropical countries—China, India, etc., and also in Egypt—and has been seen in this country in persons coming from those parts.

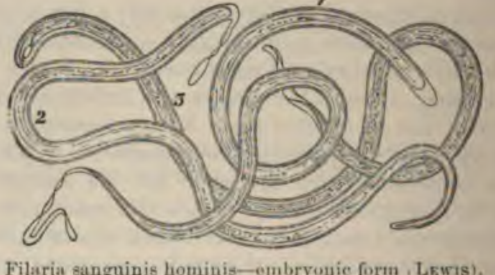
It is known in the embryonic and in the mature state, the former being found in the blood and urine; the latter in lymphatics.

The mature form has rarely been seen, and, as in the case of trichina, was discovered some years after the embryo.

The adult female is thus described:

"A long, slender, hair-like animal, quite three inches in length, $\frac{1}{100}$ inch in breadth, of an opalescent appearance, looking like a delicate thread of catgut animated and wriggling. A narrow alimentary canal runs from the simple club-like head to within a short distance of the tail, the remainder of the body being entirely occupied by reproductive organs. The vagina opens near the head and divides into two uterine horns, which, stuffed with embryos in all stages of development, run backward nearly to the tail. Under the microscope fully formed embryos can be seen escaping from the vagina. The animal is therefore viviparous" (Manson).

FIG. 95.



Filaria sanguinis hominis—embryonic form (LEWIS).

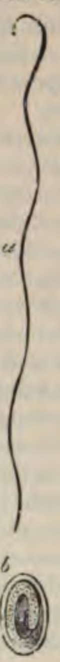
The adult worm lives in lymphatic vessels, which are apparently always dilated. How it gets there is not clear, but it is almost certainly through drinking-water that it enters the stomach of man;

bores through the walls, and instinctively makes its way into some lymphatic structures, where probably the much smaller male lodges, and the embryos are thus discharged at once into the lymph-stream; where under certain circumstances they pass into the blood.

The embryo is formed from an egg, in which it is coiled, and has the peculiarity of not bursting the chorion or egg-sac, but only stretching it lengthwise when it uncoils itself for active life, being born in it, like an infant born with a caul. The ovum coiled up in its sheath measures about $\frac{1}{500} \times \frac{1}{750}$ of an inch.

When born the embryo worm is about $\frac{1}{75}$ inch long and $\frac{1}{3500}$ in thickness, or just the diameter of a red blood-disk. It has a rounded head and a tapering tail. Its sheath or persistent chorion is about one-third longer, and trails behind as the worm moves forward, being loosely attached. The embryo undergoes no further development in the human body.

Fig. 96.



Filaria sanguinis hominis (Bristowe, after Cobbold).

a, mature female (natural size); *b*, ovum, × 250.

The presence of embryonic filariæ in the blood is subject to remarkable diurnal variations.

Generally speaking, none is to be found in the blood drawn during the daytime; about six in the evening they begin to appear, and gradually increase till, by midnight, 100 or more may be counted in every drop of blood. They then become gradually fewer, till, by eight or nine A. M., they entirely disappear, and none will now be found until next evening.

This law has been found, by Dr. Mackenzie, to be in one case altered, and even reversed, when the patient sat up all night and slept in the day. It is calculated that thirty or forty millions of embryos may be present in the blood at once. Where they lodge when not in the blood is not clear, but probably in the lymphatics.

Dr. Manson has shown that this periodicity is related, in an extraordinary manner, to the visits of a species of mosquito, which sucks and carries away blood containing filariæ. It then seeks some water, and deposits its eggs (for in this species only the female mosquito sucks blood) and dies. The embryo filariæ undergo development in the body of the insect, and when set free in the water soon become perfect filariæ. How they get back to the human body is not proved, but most likely through drinking-water. It is clear that a single pair or one gravid female will be enough to produce all the phenomena above described.

Symptoms.—The most prominent symptom is chyluria, the mixture of chyle with urine. Blood is sometimes present also. Filarial embryos are found in the chylous urine, and are doubtless the cause of the disease, though the precise manner in which chyle gets into the urine is obscure.

The condition called lymph-scrotum or nævoid elephantiasis (see p.

207) and, very probably, ordinary (fibrous) elephantiasis of scrotum or legs, are due to the presence of filariæ. These diseases depend upon obstruction of lymphatics, with production of anastomoses; which obstruction is caused, according to Manson, by the filariæ in the following way:

If an embryo is born coiled up in its sheath, instead of being extended, it has (as mentioned above) a much larger transverse diameter, being oval or spheroidal.

Hence it will be unable to pass through lymphatic glands, and will block the lymph-vessels like an embolus. This has been observed by Manson, who regards the extrusion of ova not uncoiled as a sort of abortion of the parent worm. Nearly all the people (in China) who have lymph-scrotum or elephantiasis, have also filariæ in the blood at night.

This formidable disease, endemic in countries where the filaria occurs, may therefore with much probability be attributed to it, though the sporadic cases of elephantiasis seen in Europe must have another origin.

Filaria Medinensis; Guinea-worm. (Synon.: Dracunculus medinensis.)—A worm of which the female only is known. It measures one to six feet in length, or even more, about one-tenth of an inch in thickness; body uniformly cylindrical, with a curved and abruptly tapering tail, and a rounded head in which is a simple central mouth surrounded by four equidistant papillæ, arranged conically and leading into a simple intestinal canal.

The uterus occupies almost the entire cavity of the body, and is filled with young filariæ which are born alive. No one has been able to find any genital orifice, so that if there really is not such an opening, the young must escape only by rupture of the body of the mother, or after her death.

The young worm is about $\frac{1}{30}$ inch long, and $\frac{1}{1000}$ or $\frac{1}{2000}$ in breadth. It has been shown by Fedschenko that it lives parasitically in an intermediate host, some species of cyclops, a small fresh-water crustacean. After two changes of form it becomes mature and enters the human body by the digestive organs with drinking water. Whether the two sexes enter enclosed in the body of the cyclops and copulate in the human intestine, or whether the impregnated female alone enters the human body, is not known. The female, after impregnation, makes her way through the tissues to the skin, especially of the feet and legs, as being the parts which come in contact with the mud or water where the young worms will meet with their intermediate host. When lodged under the skin it grows rapidly, and in about a year attains the great size mentioned above, when it is charged with embryos ready to go through the same cycle; and these are discharged along with the pus of the abscess which the parent worm, if left alone, produces.

As is well known, various expedients are resorted to, to extract the worm by gentle means without rupture, since if it be broken, a multitude of embryonic worms are set free, which irritate the surrounding tissues, causing severe inflammation (Davaine).

This worm is found in certain parts of India, on the banks of the Ganges; also on the shores of the Red Sea, the Persian Gulf, and the Caspian; in Upper Egypt, Abyssinia, and the Guinea Coast. It is especially prevalent after heavy rains in marshy or muddy localities, in ponds, tanks, etc.

Trematoda or Flukes.—These are soft, usually flat worms, distinguished by possessing certain pores or suctorial openings. The intestinal canal has only an oral, not an anal orifice. They do not spend their whole life in one host, but partly in an intermediate host, in intermediate forms called *sporocysts* and *rediæ*, and partly for a time in a larval state, called *cercariæ*.

The cercariæ become encysted on grass or other plants, and in that form are eaten by the species of animal which was their original host.

Distoma Hepaticum or Fasciola Hepatica.—*Liver Fluke.* The mature parasite inhabits the livers of ruminants, especially of sheep, and very rarely of man.

It is a flat, "leaf-shaped," brownish-yellow creature, which when full-grown is an inch or less long, by one-half an inch wide. It has two suctorial disks, one at the head, in the centre of which is the mouth, and one on the ventral surface. These are organs of locomotion and adhesion. The genital orifice is above the ventral pore. The organs of both sexes are united in one individual. The eggs are relatively large, oval, $\frac{1}{200}$ inch × $\frac{1}{300}$ inch, with a highly refracting shell.

The egg gives exit to a somewhat conical, ciliated, free swimming embryo. The intermediate host in which this undergoes development was long unknown, but has now been found to be a fresh-water snail, Limnæus truncatulus. The embryo fluke penetrates the body of this snail and there becomes converted into a "sporocyst." Within this are formed a large number of the intermediate forms, called *rediæ*, which leave the sporocyst and find their way to the liver of the snail, on which they feed.

The "rediæ" reach the length of $\frac{1}{18}$ inch, and within each of them is formed one of the tailed larvæ or cercariæ which, as they become mature, leave the rediæ, pass out of the body of the snail and attach themselves to the stalks of water-plants or stems of grass on damp ground.

Here they become stationary and surround themselves with cysts $\frac{1}{100}$ inch in diameter, and being eaten in this state by sheep become liver-flukes (A. P. Thomas).

The eggs formed within the body of the parent fluke find their way into water or on to grass after the death of the sheep and putrefaction of its carcass. From them are produced the ciliated embryos above mentioned.

The liver-fluke is very common and destructive in sheep, producing the disease called the "rot," from which in one year (1879–'80) three million sheep perished in the United Kingdom. It affects other herbivorous animals, and very rarely, man, who acquires it through eating water-cresses or similar plants. It lodges chiefly in the liver and causes obstruction of the bile-ducts. In man it has sometimes been found in abscesses under the skin.

Distoma (Fasciola) lanceolatum is a similar, smaller species.

Bilharzia Hæmatobia or Distoma Hæmatobium.—Bilharzia shows important differences from distoma. The sexes are separate, and differ in shape and size. The male is about half an inch long, the female four-fifths of an inch, but much narrower, being thread-like in appearance. The male has a cavity called the gynæphoric canal, occupying the hinder part of its body, in which the female is contained during copulation.

The eggs are oval or pear-shaped, and have a spine either at one end or at the side. They give rise to ciliated embryos which swim freely in water.

The mature worm is a blood-parasite, affecting men and monkeys who no doubt acquire it by means of drinking water. It is found only in the blood of the portal, hemorrhoidal, mesenteric, and vesical veins.

Here the sexes unite, and ova are produced which pass through the walls of the bladder and of the colon. Ova with *terminal* spines are found in the former, those with *lateral* spines in the latter.

On the mucous surfaces of these tracts inflammation and hemorrhage are set up, so that hæmaturia is a constant and generally the most important symptom. The eggs may often be recognized in the urine and give the diagnosis of the disease. In the bladder they are a frequent cause of calculus.

A kind of dysentery results from the irritation of the ova in the colon. By both these channels the ova pass out of the body into water and form ciliated larvæ, but the further development is unknown.

This parasite is extremely common in Egypt, where half the fellah population are said to suffer from it; also in Abyssinia, the Cape, and Natal, where it gives rise to endemic hæmaturia.

In this country it is only seen in patients who have brought it from Africa.

CHAPTER XLII.

CESTODA OR TAPE-WORMS.

Two families are distinguished, *Teniadæ* and *Bothriocephalidæ*.

The parasites thus called possess the remarkable property of exitsing in two very distinct forms, namely, as a compound jointed colony, called a "worm," and as a cystic parasite. The forms are so different that for a long time the connection between them was unsuspected. They are, however, alternate generations of the same animal. The tape-worm, by sexual reproduction, produces eggs which develop into cysts or bladder-parasites, and the latter, by gemmation, produce larvæ or scolices, each of which is capable of developing into tape-worm. These alternate forms do not, as a rule, live in the same animal. The tape-worms live in the intestines, especially of carnivorous animals, while the cystic parasites are found in the flesh or tissues of herbivorous animals which serve as food to the former class.

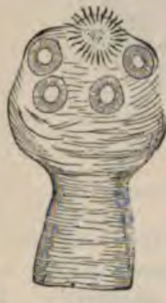
Man, being partly herbivorous and partly carnivorous, has the unfortunate privilege of giving lodgement to both kind of parasites; but the two forms of the same parasite are hardly ever found in the same body at the same time, though it is possible for the one to be developed out of the other without passing through some other body. It is usual, though not absolutely essential, for the two animals which successively lodge the tape-worm to be of different species.

The man or animal in whose body a tape-worm lives is called his "host" or "bearer," and if there is any other animal through which the parasite has to pass in order to complete its development before returning to the original host, this animal is called the "intermediate host." It will be evident from the history of certain species of parasites that their existence depends upon the relations which obtain between man and the domestic animals. Man eats the flesh of pigs and cattle containing bladder-parasites, and thus acquires tape-worm. On the other hand, he takes in water or raw vegetables contaminated by animals infested with tape-worm, and thus gets the cystic parasites. If man were the only kind of "host" available for the latter form, the species would soon become extinct.

A complete tape-worm consists of a so-called "head" and segments, or proglottides. The former structure possesses suckers, or hooks, by which it attaches itself to the intestines of its "hosts," but has no digestive organs or sexual apparatus. By a continual process of budding it forms segments, which remain attached to one another and thus constitute the long chain called tape-worm, so that the oldest or ripest segments are thus farthest from the head. Each segment when it reaches maturity has both male and female sexual organs, and produces eggs by union with another proglottis. When the eggs are matured the proglottis drops off spontaneously from the compound worm and is then ejected from the body of his "host." No part of the tape-worm contains any digestive organs, the absorption of food taking place apparently by the general surface. The development of the ova takes place while the proglottis is still within the body of its host, so that when it escapes, or when it is ejected, it is full of active embryoes, each of which is, however, still enclosed in the membrane. By the decomposition of the proglottis the embryoes are set free in water and thus have an opportunity of finding their way into the stomach of some animal drinking the water. When arrived there the enclosing membrane is dissolved by the gastric juice and the embryo liberated. It at once attaches itself to the wall of the stomach or intestine and penetrates this by means of the boring apparatus of six hooks with which it is provided. It probably enters the circulatory system by perforating a minute vein, and is then carried by the blood to the liver or some distant part of the body, or else may pass directly through the tissues. Arrived at its new habitat the active embryo loses its hooks, becomes sessile and develops into a cyst or bladder called cysticercus or hydatid, as the case may be, which is very much larger than the original embryo. After a time a bud appears on the inner side of the cyst, which ultimately develops into a scolex, precisely resembling the head of the original tape-worm. In the case of the hydatid or echinococcus-cyst numerous heads are produced by an indirect process, which will be afterwards described. Now this stage of development, it should be remembered, occurs within the body of animals such as oxen, sheep and rabbits, which serve as food for other animals. The flesh containing these bladder-parasites is eaten by some carnivorous animal or by man. The cyst containing the scolices is digested in the stomach and the little animals are set free. They attach themselves to the intestinal walls, without perforating or wounding them, and each becomes, or may become, the head of a tape-worm. The segments of this tape-worm, again, produce embryoes, which, when ejected from the bowels, will go through the cycle already described. In one species only the usual or normal mode of occurrence in the human body is the cystic form, and the tape-worm form is found in another animal—namely, in the dog. We must now speak of the different species which, in one form or another, infest man.

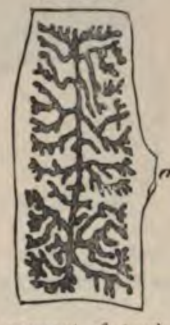
As was natural, the cystic and tape-worm forms were originally regarded as quite distinct kinds of animals. The real connection between them, however suspected, could only be proved by experiment. Pigs fed with proglottides of tænia solium develop measles in their flesh. Similarly Leuckart administered proglottides of T. mediocanellata to calves, which, when killed, were found to have the cysticercus of this species in their muscles. Küchenmeister examined the body of an executed criminal, who, two or three days before his death, had eaten measly pork, and found free scolices or tape-worm-heads in the intestine. A French experimenter even succeeded in developing tape-worm in himself by eating cysticerci derived from the human body.

FIG. 97.



Head of tænia solium, magnified (after HELLER).

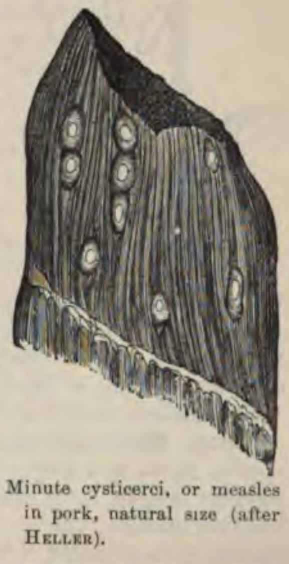
FIG. 98.



Mature segment of tænia solium, showing the ramified ovary (after HELLER). *a*, genital pore.

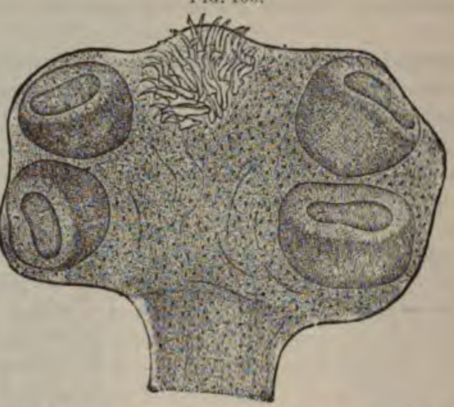
Tænia Solium and Cysticercus Cellulosæ.—(*Etymology:* Cysticercus telæ cellulosæ, or bladder-worm of the cellular membrane.)—This species infests man in both stages of development. The tape-worm, when full-grown, may be three or four yards in length. The head is not larger than the head of a small pin. It is furnished with four suckers and a circle of about twenty-six hooks supported on a rostellum. The first portion of the body of the worm is narrow and threadlike, but it soon enlarges and becomes transversely segmented. The segments are at first broad and very short: afterward their length is greater than their breadth. When it has attained the length of some five feet and produced 450 segments, sexually mature proglottides are produced, each having male and female organs, the genital orifice being situated laterally on the right and left side alternately. The ovary has from seven to ten lateral branches, each of which divides into dendritic ramifications. The eggs are nearly spherical, about $\frac{1}{750}$ of an inch in diameter. The partly developed embryo, with six hooklets, may be seen within it. The further development takes place in the manner already described, in the flesh of pigs. The bladder-parasite there produced is called a measle, or cysticercus cellulosæ. The meat thus affected is called "measly," and shows to the naked eye a number of little bladders the size of a pea, or somewhat larger when full-grown. It requires two or three months to attain this size, and it is supposed that it may

FIG. 99.



Minute cysticerci, or measles in pork, natural size (after HELLER).

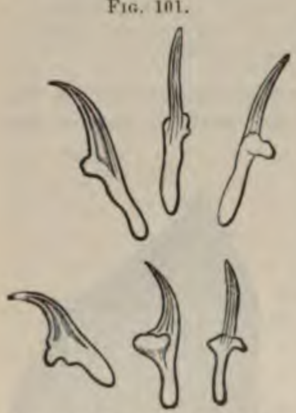
FIG. 100.



Head of cysticercus cellulosæ (highly magnified).

live in the cystic form for several years. If the cysticercus dies, its body becomes calcified, so that a chalky mass results, surrounded by a fibrinous membrane. The tape-worm form of this parasite is only known to occur in man. It is always acquired by eating imperfectly cooked pork. The cysticercus form occurs in enormous abundance in the pig. It is sometimes found in the human body, mostly in the muscles, but also in the brain and bone and skin, etc. It is not often that, in the human subject, more than one is found; but as many as twenty have occurred in the brain, and even hundreds in muscles and connective tissue. If degenerated or decomposed, it may be recognized by the presence of the hooklets, which should be distinguished from those of T. echinococcus or hydatids. Those of the cysticercus are larger, and have a characteristic shape (*see* Fig. 101). We must suppose that the cysticercus is acquired by drinking water which has been contaminated with matter containing tape-worm eggs. It is possible for a person having a tape-worm to infect himself, by indirect means, with cysticerci from his own parasite.

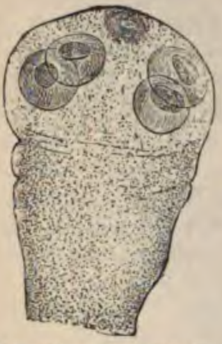
FIG. 101.



Hooks of cysticercus cellulosæ.

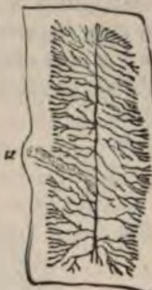
Tænia Mediocanellata, vel Saginata; Beef Tape-worm.—This species grows to a larger size than tænia solium, being sometimes four yards in length. Its head is about one-eighth of an inch in diameter, has four suckers, but no hooks or rostellum. It tapers slightly to a narrow portion called "the neck," after which it rapidly enlarges and forms distinct segments. These may be as much as three-fourths of an inch long. The ovaries of this species give off a very large number of lateral processes, which do not branch in the same way as in T. solium, but form parallel twigs. This is the only characteristic by which the segments of the two tape-worms can be distinguished. The segments of T. mediocanellata have more power of spontaneous movement than those of T. solium, and may thus leave the intestine independently; while joints of the latter form are discharged, as a rule, with the feces. The mode of reproduction and of development of the embryo is the same as in T. solium, except that it develops in the bodies of cattle instead of pigs. Man consequently acquires this parasite by eating underdone beef. Although T. solium is generally spoken of as the common tape-worm, I believe the present species to be now commoner in this country—at all events in London. I have seen a great many specimens from hospital out-patients, although for some years I have not seen any of T. solium. The cysticercus form appears to occur in cattle only, never having been found in other domestic animals or in man. It is found singly or in small numbers; and does not exceed one-third of an inch in diameter.

FIG. 102.



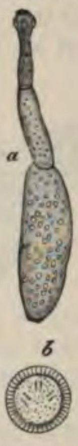
Head of tænia mediocanellata, magnified (after HELLER).

FIG. 103.



Mature segment of tænia mediocanellata, showing arrangement of lateral processes of ovary. *a*, genital pore.

FIG. 104.

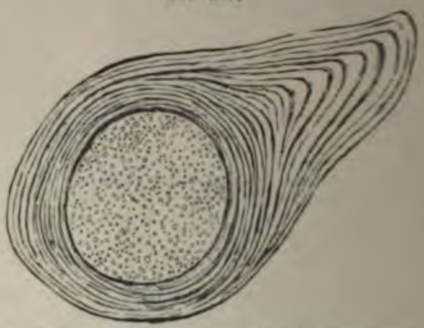


Tænia echinococcus (after BRISTOWE). *a*, tænia (× 10); *b*, ovum (× 250).

Tænia Echinococcus; Hydatid Cyst.—This is found as a human parasite only in the cystic form. The tape-worm lives in the intestines of the dog and wolf. It is about a quarter of an inch long, and consists of four segments only, including the head. The head is pointed, has a double circle of hooklets, thirty or forty in number, and four suckers. The final proglottis, when mature, is equal in size to all the rest. It has a lateral genital pore and complicated ovaries, containing numerous eggs (about five thousand it is supposed), in which develop the six-hooked embryos.

When this ripe segment drops off, the embryos are set free on the surface of the ground, or in water, by which (or on the surface of green vegetables eaten uncooked) they may pass into the human stomach. Perforating the walls, they get into the circulation, and hence, for the most part, pass to the liver, though occasionally they lodge themselves in other parts. When the embryo becomes stationary, it develops into a spherical vesicle, which undergoes various changes, and may become of great size. This, the bladder-form of the parasite, is known as acephalocyst or hydatid. It is surrounded by a secondary fibrous envelope formed from the tissues of the host.

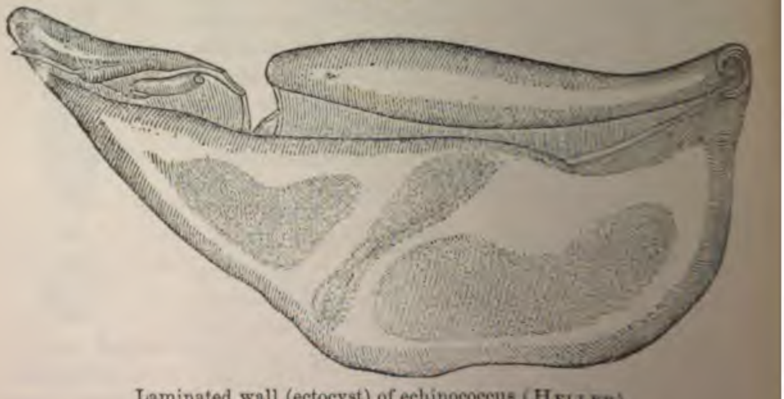
FIG 105.



Section of small hydatid cyst (× 100) (BRISTOWE).

The subsequent development of this cyst is very remarkable, and unlike that of cysticercus. After about eight weeks, when it is one-fifth of an inch in diameter, it consists of a thick *laminated* membrane externally, enclosing a granular mass. This mass then forms a layer of nucleated cells on the inner surface of the laminated membrane—the so-called granular layer—while central parts contain fluid

FIG. 106.



Laminated wall (ectocyst) of echinococcus (HELLER).

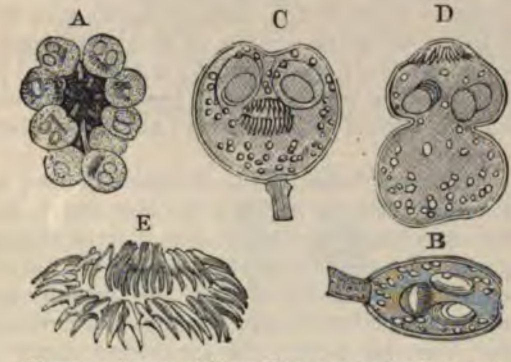
There thus results a cyst with a double wall, the outer laminated or *ectocyst*; the inner protoplasmic, called the *endocyst*.

When the cyst reaches the size perhaps of a walnut, the production of scolices, or echinococcus-heads, begins, as follows:

In the substance of the endocyst, buds are formed projecting into the cavity, and forming a structure termed a brood-capsule, in which the position of the two layers in the original cyst are reversed; having the parenchymatous layer on the outside, the fibrous or ectocyst inward, so that it is like an invagination of the cyst-wall. On the outer side of this are formed the echinococcus-heads or scolices, which therefore project into the cavity, though by doubling inward of the wall of the brood-capsule they often appear to be inside of the latter. They do not become free in the cavity, unless they die, but brood-capsules may be formed in such numbers as nearly to fill the cavity.

If the process goes on as described, the development possible in this situation is complete. The head, or larval tapeworm is formed; and if the organ in which it is lodged be eaten by a carnivorous animal, it may at once enter on the tape-worm stage of existence. This result has been produced experimentally by feeding dogs with hydatids.

FIG. 107.



Human echinococci (from FINLAYSON, after DAVAINE).

A, a group of echinococci, still adhering to the germinal membrane by their pedicles (× 40).

B, an echinococcus with head invaginated in the body (× 107).

C, the same compressed, showing the suckers and hooks of the retracted head.

D, echinococcus with head protruded.

E, crown of hooks showing the two circles (× 350).

The echinococcus-head or scolex is $\frac{1}{60}$ to $\frac{1}{100}$ of an inch in length. Its body is divided into two parts—the anterior, called the head, which carries a rostellum with hooks and suckers, and the posterior part, or base. The head (which is, of course, identical with the head of the little tape-worm in the dog (has two circles of hooks, which should be carefully studied, since the discovery of even one may be the means of diagnosis. The smaller measure $\frac{1}{1040}$ to $\frac{1}{1780}$ of an inch; the larger $\frac{1}{830}$ to $\frac{1}{1780}$ (Cobbold). As we see in the scolex, the head is generally retracted into the body, so that the hooks appear as if they were internal organs. The calcareous corpuscles, which are found in this as in the mature tape-worm and the hydatid, also often serve as a means of diagnosis.

The process of development does not always, however, go on at once to the production of scolices. The mother-cyst may instead produce secondary or daughter-cysts, so that scolex-production is deferred.

These secondary cysts are formed in three ways. One mode of formation, common in hydatids of domestic animals, but rare in man, is the exogenous, producing the form called Echinococcus veterinorum, or E. exogenus, or E. granulosus. Secondary cysts are formed in the wall of the original, which grow outward; and thus a collection of cysts, lying side by side, not enclosed in one, is formed. The secondary cysts have the same power of forming "heads" in their interior as the primary cyst.

Another mode, the common one in human hydatids, is that daughter-cysts are formed, sometimes in enormous numbers, inside the mother-cyst; and sometimes others within these (granddaughter-cysts). This form is called Echinococcus endogenus, or E. hydatidosus.

A third form, unknown in this country, is that called by Virchow Echinococcus multilocularis; which, as it has a very limited geographical range, being only found in Switzerland and South Germany, need not be further described.

In the only important human form of echinococcus-cyst (E. hydatidosus) the daughter-cysts are abortive brood-capsules, and probably abortive echinococcus-heads also, which stop short at this stage instead of developing normally; but the causes of this arrest of development are quite unknown. Probably, at first, the daughter-cysts have a granular parenchymatous layer, and are capable of forming heads, but a great number lose this power, and are barren cysts. When the daughter-cysts are very numerous (thousands are described) many or even all may be barren. Leuckart doubts whether all are so; but certainly I have examined very large numbers without finding any heads or hooklets, and many similar experiences are recorded. Sterile cysts have a thick, white, opaque wall.

Echinococcus-cysts in man may be very large (15 lbs. or more); the fluid they contain is watery, containing sodium chloride, but scarcely a trace of albumen, a point of great diagnostic importance. When they die, this fluid becomes inspissated, and with the secondary cysts, etc., forms a gelatinous or sometimes cheesy mass. In the end this may become calcified, as may also the wall, a tendency to calcareous deposit being very marked in hydatids.

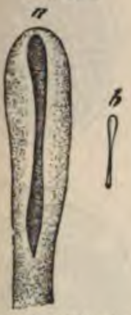
The liver is the seat in about one-half of the cases; next in order of frequency come the lungs; and hydatids do occur also in the peritoneum, brain, heart, muscles, etc. I believe statistics underrate the frequency of cases in the liver, as cases in other situations, being varieties, are published. Migration within the body is doubtful; except perhaps from liver to peritoneum.

The cysts may burst into some natural cavity, and thus be evacuated, or they may be destroyed by suppuration of the external envelope of human tissue. The various events which thus result belong to special pathology.

Bothriocephalus Latus (*Tænia lata*); **Broad Tape-worm.**—The tape-worm lives in the human intestines; the cystic form is unknown, if any exists; but in all probability the embryo derived from the tape-worm develops direct into a larval form in the muscles of fish.

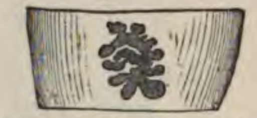
It is larger than any species of Tænia, sometimes attaining a length of twenty-five feet and a breadth of one inch. The head is very simple, $\frac{1}{25}$ inch across, with no suckers or hooklets. The joints near the head are very short and wide, looking like mere rings; the largest occur in the middle of the chain, and are not more than $\frac{1}{8}$ to $\frac{1}{4}$ inch long; toward the posterior part of the body the joints become slightly longer and narrower. There may be 4000 segments. Each is bisexual; the uterus is a simple tube, though convoluted. The genital orifices are in the middle line, on the ventral surface. The eggs are oval. $\frac{1}{350}$th inch long; they are furnished with an operculum. They are set free within the body, but hatched in water. The proglottides are not discharged from the intestine, as in Tænia.

Fig. 108.



Head of bothriocephalus latus (Heller). *a*, magnified; *b*, natural size.

Fig. 109.



Mature segment of bothriocephalus latus.

The embryo is furnished with a ciliated envelope, and swims about till this bursts, liberating the six-hooked embryo. This undergoes intermediate development in the muscles or viscera of a fresh-water fish (especially the pike) to an asexual larval worm. If such a fish be eaten by man, or other fish-eating animal, it will develop into the sexually mature form already described.

The tape-worm has been found in man, and in the dog. It has a very limited geographical range, being found commonly only in Switzerland, certain parts of Northern Germany, Russia, Poland, Sweden; occasionally in Holland and Belgium; rarely in Ireland. In England and France the few recorded cases appear to have depended upon some traveller bringing the tape-worm with him from a country where it is endemic. In short its distribution seems to be determined by the great river and lake systems.

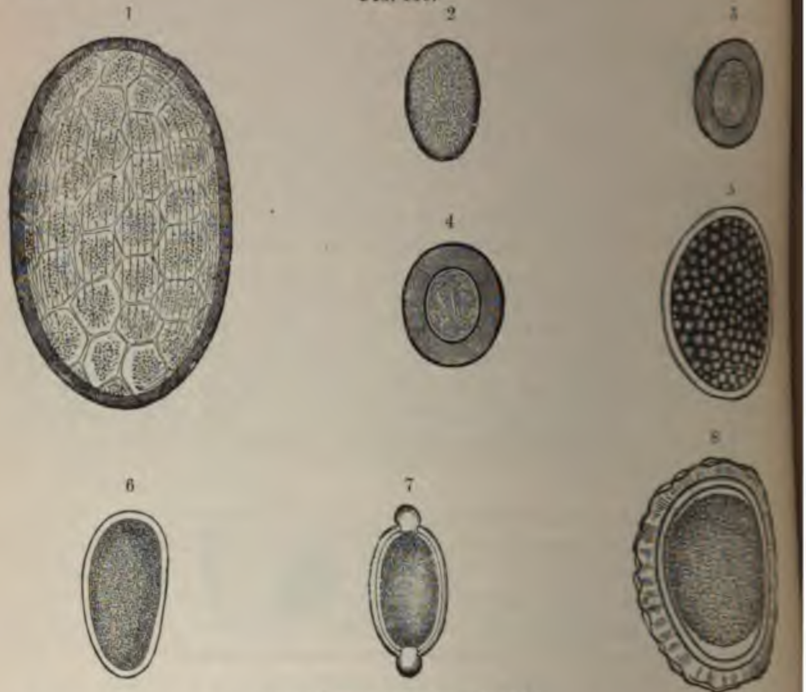
Rarer Tape-worms.—There are certain other species which have been very rarely found in man, some of them in only a single instance.

Such are: *Tænia cucumerina*, common in the dog and cat; *T. acanthotrias* (America); *T. marginata* (?); *T. nana* (Egypt); *T.*

flavopunctata (America); *T. Madagascarensis*; *Bothriocephalus cordatus* (Greenland) *B. cristatus* (?); *B. liguloides* (from Japan).

Eggs of Entozoa.—For the sake of convenient reference, the figure showing the comparative size of the eggs of different parasites is here annexed.

Fig. 110.



Eggs of entozoa (after Heller).

1. Distoma hepaticum. 2. Distoma lanceolatum. 3. Tænia solium. 4. Tænia mediocanellata. 5. Bothriocephalus latus. 6. Oxyuris vermicularis. 7. Trichocephalus dispar. 8. Ascaris lumbricoides (× 350).

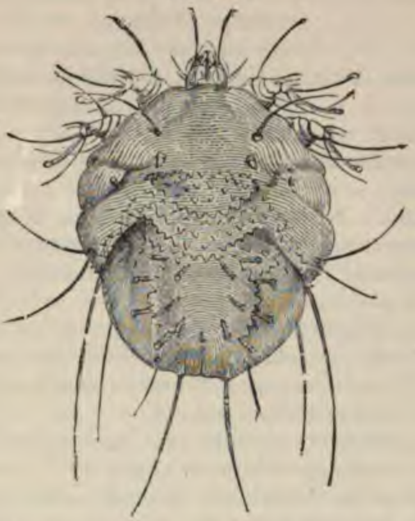
CHAPTER XLIII.

ANIMAL PARASITES—ARTHROPODA.

ARACHNIDA.

Acarus Scabiei.—The well-known parasite of the itch is a mite, of which the sexes differ in size. Its general appearance is best understood by inspection, or, failing that, by a figure, so that a long description is not necessary. The female, which is generally seen, is $\frac{1}{180}$ to $\frac{1}{60}$ inch in length and $\frac{1}{125}$ to $\frac{1}{75}$ broad; the male little more than half that size. He differs also in having the hindmost of the four pairs of legs terminated by a disk and not a bristle. In the female the two hinder pairs of legs have bristles. The two anterior pairs in both sexes have disks (see Figs. 111 and 112). The male either lives on the surface of the skin or penetrates a little way into the epidermis. He is very rarely found. The female burrows in the epidermis and lays her eggs there. The track of her burrow, as a blackish curved line, is a well-known diagnostic mark of the disease. The eggs are oval, about $\frac{1}{150}$ inch long and have a granulated surface. The young when hatched are immature, having only three pairs of

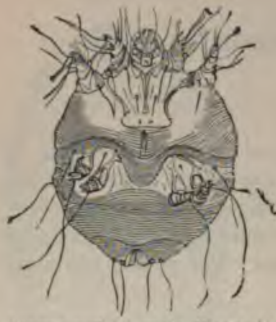
FIG 111.



Acarus scabiei, female. Dorsal aspect. (CORNIL and RANVIER.)

legs. They grow quickly, and after several changes of skin assume the perfect form. The acarus breathes air by the general surface, without special respiratory organs. It is a true parasite, not being able to live except on an animal body, though it may be transferred from one species of animal to another. Whether all the acari which infest many of the lower animals are always different from the human acarus is not clear. There are certainly some other species.

Fig. 112.



Acarus scabiei, male. Ventral aspect. (Cornil and Ranvier.)

Besides its burrows, the acarus gives rise to little vesicles *near* the burrows; but the way in which these are produced is not (to me at least) quite clear, since the acari are never found in them; but then it is possible that the acarus secretes some irritating substance which sets up local inflammation. There is little doubt, however, that the scratching, to which the intense irritation of the skin gives rise, is the chief immediate cause of the actual lesions of the skin which constitute the disease scabies. That it is extremely contagious is well known, but a somewhat close contact is necessary to transfer the disease.

Demodex folliculorum.—(Syn.: Acarus folliculorum.)

Although really an acarus, this creature has a very different shape from the A. scabiei. Its head is like an acarus, it has four short legs and a long abdomen, which give it the appearance of a worm. It is a remarkable instance of the degeneration produced by parasitism. Its average length is $\frac{1}{125}$ inch.

It inhabits the plugs of thickened sebum or comedones, produced by oversecretion of the sebaceous glands in the skin of the face, shoulders, etc. Several are often found in one hair-follicle, with the long axis of their body directed inward.

They are not known to produce any pathological change, but are nourished by the abundant sebaceous secretion.

I cannot confirm the statements generally made as to the frequent occurrence of these creatures. In cases of acne they are certainly very uncommon.

Similar parasites occur in the lower animals; and one in the dog seems to produce pathological changes, according to Sparkes.

Leptus Autumnalis, or the harvest-bug, is very common on grass or stubble, in the autumn especially, at least in this country, on chalk soils. It creeps up the leg and burrows into the skin, where it causes excessive itching. It is a bright red creature, just visible to the naked eye. As it certainly does not undergo any development in the human body, and soon dies there, it must be regarded as an occasional visitant and not a parasite.

Zoölogically, it is the six-legged larval form of an eight-legged mite, of genus *Trombidium* and species probably *holosericeum*. The larva is normally parasitic on insects and arachnida, and sometimes visits man or other mammalia.

Ixodes Ricinus, the sheep-tick, occasionally fastens upon the human body and sucks blood from it. In the lower animals it appears to be a true parasite.

Other more formidable species are known in other countries, as *Ixodes Americanus*, in Brazil.

Pentastomum Tænioides seu Denticulatum also belongs to the class Arachnida, though very different in appearance to most species of that class.

The larval form only is met with, in an encysted form, as a rare human parasite, but is common in the rabbit. It is about $\frac{1}{5}$ inch long and $\frac{1}{15}$ broad; has a roundish, flattened body, divided into some ninety segments, after the manner of a tape-worm, but the division is only superficial. The edges of the segments are bordered with fine bristles and in the middle of each are stomata. The mouth is surrounded by four hooks, each provided with a chitinous sheath into which it can be withdrawn. It is enclosed in a capsule making a nodule the size of a pea, mostly in the liver.

In the human body it is generally found dead and calcified, the contents of the capsule being merely a calcareous paste in which the hooks may sometimes be found entire.

Leuckart has proved it to be the larval form of an arachnoid, the mature form of which is known as *Pentastomum tænioides*. The female is about three inches long, the male less than one inch. It lives in the nasal cavities and frontal sinuses of dogs and wolves. The embryos still contained in the egg membranes pass out with the nasal mucus onto plants, and thence into the stomachs of rabbits and hares, where, becoming free, they pierce the intestinal walls and reach the liver. In this organ they become encysted and pass through a series of changes of form till the pentastomum denticulatum stage is reached, when they commence a fresh migration to other organs—an operation sometimes fatal to the host. If the body of the hare or rabbit be now eaten by a dog, the embryos pass from its mouth into the nasal passages and in two or three months are sexually mature.

In one case the mature parasite was found in the nostril of a man who had suffered for seven years with severe bleeding from the nose.

INSECTA.

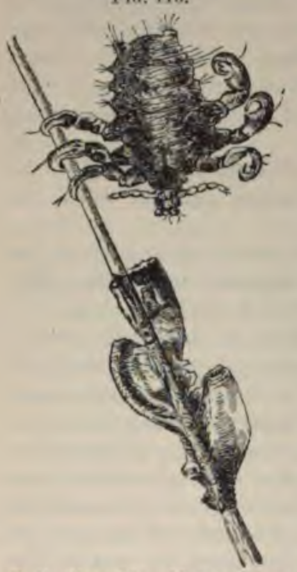
The most important parasitical insects are lice, of which three species infest the human body:

Pediculus capitis, *Pediculus vestimentorum* and *Pediculus* (phthirius) *pubis*.

Pediculus Capitis, the head-louse, lives in the hairy scalp and is supposed to suck blood from the vessels around the hair-follicles. The female attaches her eggs or *nits* to the hairs by a peculiar arrangement something like a split ring, and fastens them with a chitinous cement, so that they are with difficulty removed, even when the young are hatched, which is said to occur in about a week. The young have six legs, like the mature insect, and undergo no metamorphoses. The appearance of this creature need hardly be described, but it may sometimes be important to distinguish between this and the next species. The most obvious difference is that the body of the head-louse is mottled with gray or black, so that it precisely resembles a dirty piece of scurf. The clothes-louse has no local color, but is of a general dirty white, and the blood which it has swallowed is often seen through the skin.

Pediculus Vestimentorum, the clothes or body-louse, lives in the clothes or bedding, and lays its eggs in the folds of garments. It makes excursions upon the body, and sucks blood from the vessels surrounding the sebaceous glands and hair-follicles; especially of those parts of the body (such as the shoulders and waist) where the clothes fit most tightly. The puncture thus produced may be recognized.

FIG. 113.



Pediculis pubis. Mature insect eggs attached to a hair (FINLAYSON).

The irritation the lice produce, and the lesions set up by scratching, often gives rise to the erroneous diagnosis of a disease "Prurigo," which is really quite a distinct affection.

The affections produced by lice are sometimes called phthiriasis, and in former times this was thought to be a disease produced by internal causes, and fabulous stories were told of its disastrous and even fatal results. Modern dermatologists repudiate the possibility of lice living in or under the skin in ulcers and abscesses. Nevertheless a preparation from Schröder van der Kolk's collection, now in the University Museum at Oxford, proves that this is not impossible. It shows the arm of a person affected with phthiriasis, the skin being riddled with ulcers and subcutaneous cavities, which during life were full of lice.

When large numbers of lice are found on the body after death, as sometimes happens, these are head-lice, which have swarmed over the body after death.

Pediculus Pubis.—This differs much in form from the other species, so that it has received the generic name *Phthirius*. Its general appearance is shown in the figure. This species inhabits those parts of the body covered with short hairs, especially the pubes; but is found more rarely in the axilla or on the eyebrows, or among short hairs on the chest. The female attaches her eggs to hairs in the same manner as the head-louse.

Other species of insects live as occasional epizoic parasites.

Cimex Lectularius, the bed-bug, is a wingless species of the order Hemiptera. Its development takes place outside the body, which it visits only for the sake of sucking blood.

Pulex Irritans, the common flea, is also a wingless species belonging to the order Diptera. Its larva, a bristly cylindrical worm about one-eighth inch long, goes through its pupa-stage on the ground, in dry soil or sand, and probably in the dust of dirty floors. In one extraordinary case it was found in numbers on the human body. I have been informed by a traveller in Persia that he has found whole villages depopulated in summer, through the inhabitants camping out in the woods, to avoid the fleas which infested their houses. The flea is rather a house-pest than a parasite, and the same may be said of the bed-bug.

Pulex or Sarcopsylla Penetrans.—The sand-flea or chigoe lives free in sand in parts of North and South America. The pregnant female seizes any opportunity of burrowing under the skin of accessible parts, such as the feet of quadrupeds or men. In the latter, the skin of the toes under the nails is usually selected. Here she swells up from one-twenty-fifth to one-fifth of an inch in diameter, and becomes nearly spherical. She then extrudes her eggs one by one, and, when this process is completed, dies. If the creature is left alone, no great harm is said to result; but if irritated or crushed, severe inflammation and suppuration are set up.

Occasional Insect Parasites.—A few other species of insects are in the larval form occasional parasites of men.

Thus certain flies, especially the bluebottle and other large species, occasionally lay their eggs in neglected wounds and ulcers, when the maggots developed from them may cause severe and even fatal injuries. A few instances are known of maggots making their way through the skin into the muscles of the living body, under peculiar circumstances, as for instance, from putrid meat, and even causing death. The maggots of one species of fly in South America, *Lucilia hominivorax*, normally live as parasites in the nostrils and frontal sinuses of men; whence they may bore their way into the pharynx and other adjacent parts, causing severe inflammation.

CHAPTER XLIV.

VEGETABLE PARASITES.

THE forms of vegetable life which occur as parasites in or upon the human body, belong, as may be supposed, exclusively to the lower orders of plants. This, indeed, necessarily follows from the fact of their drawing their sustenance from animal fluids and tissues. For the physiological distinction of the higher plants which possess chlorophyll is that they are able to decompose carbonic acid and build up their tissues from the gases of the atmosphere and inorganic matter, very rarely feeding on organized materials. The lower plants, on the other hand, obtain their nutriment after the manner of animals, from more complex materials, such as are or have been parts of living organisms, which materials they break up to form their own tissues. The absence of chlorophyll is broadly a sign of this physiological difference; and though not absolutely distinctive, is generally characteristic of the lower plants of which we are speaking. Without pretending to give accurate botanical definitions, we may say that all parasitic plants belong to the group of achlorophyllous thallophytes, generally called fungi, and may be classified under three subdivisions of this group, viz., *hyphomycetæ* or mould-fungi, *blastomycetæ* or yeast-fungi, *schizomycetæ* or fission-fungi, generally called bacteria.

Species belonging to each of these are known either as true parasites, which necessarily spend the whole or part of their lives in or upon the human body, or as occasional parasites which visit the human body only occasionally, generally living an independent life. The structure of the true parasites, as compared with that of the most nearly allied species living an independent life, sometimes appears to show the degeneration of parasitism referred to in speaking of animal parasites. The moulds, for instance, which live on the human skin, and produce certain well-known diseases, have a much simpler structure than the common blue moulds which they in some respects resemble.

Just as we distinguished entozoa from ecto- or epizoa, so we may distinguish those vegetable parasites which are capable of living inside the body as *entophytes*, and those which merely grow on the surface as *epiphytes*, though the former term is less frequently employed than the latter.

The effects produced by vegetable parasites, though as a rule, very different from those of animal parasites, are very various. Some live merely on the food substances or waste products of the body, without producing any pathological changes, and are then called *Saprophytes*; others, the *Pathogenic* species, produce inflammation and necrosis changes at the spot where they grow, as well as formidable general diseases.

The most important factor in the deleterious action of parasitic plants, and that which chiefly distinguishes their effects from those of animal parasites, is that they often set up injurious chemical decompositions or fermentations in the tissues and fluids of the body; and by so doing they not only destroy the vital properties of those tissues and fluids, but also give rise to new chemical substances which are of the nature of poisons; some being tissue poisons, some functional poisons (as formerly defined), which substances being distributed by the blood may cause destructive changes in distant parts or dangerous functional disturbances of the nervous system.

As in the case of parasitic animals so with parasitic plants, there are usually certain laws which regulate their entrance into and their exit from the body. Epiphytes, like epizoa, are often mechanically transported from one individual to another, so that ringworm, for instance, an epiphytic disease, is also contagious, in the same way as the tape-worm disease may be said to be contagious. Endophytic parasites, like entozoa, enter by some regular channel to which their habits of life are strictly adapted, and for the most part leave the body by some equally regular method, which permits them to pass directly, or indirectly, into some other host, so that the species may be continued. The laws of external existence of parasitic plants are much less perfectly known than in the case of animals, but it is clear that in some species their vitality is maintained by *spores* which have greater powers of resistance than the mature plant, and may thus be compared to the eggs of animals, *e. g.*, of the tape-worm. This is the case, for instance, with the bacillus of anthrax, which after living in the blood and tissues of cattle in the form of long threads, produces spores, which, when they leave the body, are able to preserve their vitality in grass or soil till the opportunity occurs again of entering an animal body.

Vegetable parasites, perhaps more often than animal, cause the death of their host; but the organism just mentioned supplies a remarkable instance of how this event is adapted to the laws of life and continued existence of the parasite. When a sheep, for instance, dies of anthrax on a pasture, and the carcass is allowed to remain on the spot, the soil will become infected with the spores of the bacillus, both by means of its excreta, blood, mucus from the mouth, and so forth; and also under certain conditions, from the carcass itself; the contagium being thus preserved to infect other animals. This case presents a close parallel to that of the liver-fluke (p. 415), which kills its host, the sheep, and by that means secures the distribution of its eggs over damp grass or water, where they undergo further transformations and ultimately reach the sheep again.

Metamorphoses of parasitic plants comparable to the metamorphoses and alteration of generations in so many animal parasites, are hardly known, but it is by no means impossible that there may be, in their case too, corresponding stages of existence; and perhaps some of the forms which we know represent only one stage of the life cycle, though it appears complete, just as was the case, for instance, with cystic parasites before their connection with tape-worms was discovered.

Similarly, we know very little of any intermediate hosts in the case of parasitic plants. But many are common to several species of animals, and may be communicated from one to another mutually. Thus man often derives his vegetable, as he does his animal, parasites from other species, either domestic or wild This is true of the fungus which produces favus, of the bacillus which causes anthrax, probably sometimes of the bacillus of tubercle. But there is no case in which it is definitely known that a vegetable parasite must pass through any intermediate host before attaining its perfect development.

The difficulties which present themselves in the solution of many problems of parasitic plant-life are largely due to the imperfection of our knowledge respecting the natural history of these lowly organisms. It is only of late years that the life-history of even a few forms has been thoroughly worked out. But it must be said that nothing but the rapid advance, which has been made of late years in this difficult branch of botany, could have rendered possible the equally striking and simultaneous advance in our knowledge of vegetable parasitic diseases.

There are so few general propositions that can be made about vegetable as distinguished from animal parasitism, that it will be best to proceed at once to consider the special forms of parasitic plants.

CHAPTER XLV.

HYPHOMYCETÆ AND BLASTOMYCETÆ—MOULDS AND YEASTS.

Hyphomycetæ or Moulds are achlorophyllous thallophytes or fungi, consisting of a *mycelium* with certain organs of fructification.

The mycelium is composed of threads or filaments called *hyphæ*. The hyphæ are generally divided by septa, and are often branched. The organs of fructification consist essentially of cells called spores or conidia, which are sometimes produced in or upon more complicated structures, sometimes merely by cutting off, or "abstriction," of certain portions of the hyphæ.

In the higher forms the organs of fructification consist of upright hyphæ growing into the air, called conidiophores. These produce either true spores by endogenous formation within a structure called a sporangium, as is the case in mucor; or else divide into smaller threads called sterigmata, arranged in a brush-like form as in penicillium, or in a spherical shape as in aspergillus. The cells formed by abstriction of the sterigmata are called conidia. In some species spores are produced by a sort of sexual conjugation, as in higher plants, and there are other modes of fructification which need not be described here. In the simpler forms, under which are included all the truly parasitic and pathogenic species growing in the human body, conidia are formed direct from the hyphæ of the mycelium.

Moulds are found almost universally on decaying vegetable matter wherever the conditions of temperature and moisture are favorable to them. Their mycelium penetrates the substance on which they grow sometimes very deeply, and some species are able to penetrate very hard materials, such as wood. In doing so they decompose and destroy their vegetable soil, and their function in nature appears to be the removal of dead vegetable matter. Some species, as the potato-fungus (Peronospora), are able to attack in the same way living plants, in which they cause great destruction. These species are, therefore, pathogenic to plants.

Some moulds are capable of growing upon and causing the decomposition of dead animal matter; but they are not often found in such situations, and their importance in this respect is much less than that of bacteria. It might almost be inferred from these facts that they would have still less power of attacking living animals, and hence moulds have little pathological importance. They do, however, cause in man certain diseases of the skin, and one or perhaps two diseases of deeper parts. In these their pathogenic action is purely irritative or inflammatory. In some animals diseases from moulds or mycoses are more common. Several species also occasionally grow as saprophytes in natural or artificial cavities of the body. Certain of these saprophytes are found to produce disease if artificially introduced into the interior of the body.

The saprophytic species are identical with species growing on decomposing matters outside the body; but the pathogenic species are distinct. Before speaking of the latter, it will be well to enumerate a few of the commoner moulds which are met with in outside nature, and may occur in pathological conditions.

Saprophytic or Non-pathogenic Moulds.—The only species which it is necessary to notice here belong to the three genera Aspergillus, Penicillium, and Mucor.

The genus Aspergillus is characterized by the growth from a branched mycelium of upright hyphæ, producing spherical heads of sterigmata, on which are formed the conidia.

Aspergillus Glaucus is a common grayish-blue mould which grows on decaying fruit, rotten wood, and other vegetable matters, especially in cool places. When grown artificially, it is found to flourish at a temperature of about 50° F. (Flügge), and not at all at temperatures approaching that of the human body. Its conidia are, compared with those of other species, large, measuring 9 to 15 μ, or micromillimetres, in diameter.[1]

Aspergillus Niger, an allied species, produces, on spherical heads, conidia of a brown color when ripe, of 3.5 to 5 μ in diameter. This species grows freely at a high temperature, best at about 95° F.: therefore very nearly at the temperature of the human body.

It is sometimes found growing in the human ear, a situation for which its temperature-relations evidently fit it, and is the commonest of the species of fungi found there.

It is most commonly met with in the outer ear—sometimes on the membrana tympani, sometimes even in the middle ear.

According to Schwartze, it will not grow unless there is already some slight injury of the epidermis, but when once established it produces a severe and obstinate inflammation called Otomycosis; so that it may be called pathogenic. Other forms of fungus found in the ear are, according to Schwartze, Ascophoro elegans, Trichothecium roseum, Mucor mucedo.[2]

A species of Aspergillus, perhaps the same as this, has been observed growing in a wound of the cornea of the eye.

Aspergillus Fumigatus, an allied species, produces small conidia, 2.5–3 μ in diameter. It grows best at a high temperature, 98°–104° F. It is this species which, as already mentioned, has been made to grow in internal organs of rabbits if the spores are injected into the blood, being doubtless adapted to growth in such situations in consequence of the high temperature which suits it best. When the quantity injected has been large some general symptoms and even death have resulted. Another species, aspergillus flavus, is almost as virulent. A. niger has a much less intense action, while A. glaucus is without effect, apparently on account of the high temperature being unfavorable to its growth. In none of these experiments, however, has there been any great multiplication of the fungus within the body.

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[1] In this part of the work, to avoid the awkwardness of speaking of minute fractions of an inch, or of decimals of a millimetre, we shall use the symbol μ for one-thousandth of a millimetre $= \frac{1}{25000}$ of an inch.

[2] Schwartze, in Klebs's Handbuch der Pathol. Anatomie, 6te Lieferung. Berlin, 1878.

A species of aspergillus, probably A. fumigatus. has been found in the lungs, viz., in tubercular vomicæ, or bronchiectatic and gangrenous cavities, but without producing any disease, being only a saprophyte. An undetermined species of the same genus was once observed by Mr. Hutchinson in crusts of impetigo from the head of a child, but evidently not as the cause of the disease.

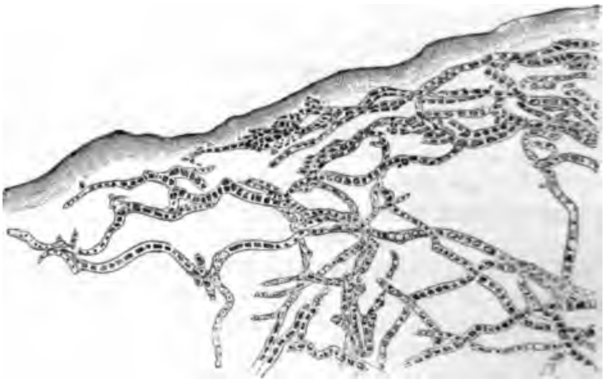
Penicillium Glaucum is the common blue mould which grows almost universally on articles of food, and all kinds of decaying animal matter in moist, dark situations. Its upright conidiophores divide into small branches so as to form a sort of brush of filaments at the end of which conidia are produced. The latter measure on an average 3.5 μ, while the threads are from 4 to 7μ in diameter. It grows well at the ordinary temperature of a room, best between 70° and 80°, not at all at the temperature of the body. Injected into animals it is entirely without pathogenic action.

Mucor Mucedo is a white mould, found mostly commonly on fecal matter, especially horse-dung. It forms a ramified mycelium in the nutritive material, and sends up fructifying hyphæ, on which spherical sporangia are formed. In the interior of these the spores are produced and are set free by bursting of the sporangium. The spores are from 8 to 37μ in diameter. If grown under the surface of a nutritive fluid mucor produces only oval cells resembling those of yeast. It grows at ordinary temperatures and also at that of the human body. Injected into animals the spores are without effect.

Two other species of the same genus, viz., Mucor rhizopodiformis and M. corymbifer, have been found by Lichtheim to be pathogenic in rabbits. If the spores are injected into the blood, after an incubation of twenty-four hours, illness is produced which causes death in two or three days. The kidneys are found greatly enlarged and containing growth of fungus-mycelium. The same is seen in a marked degree in the Peyer's patches of the lower end of the ileum as well as in the mesenteric glands and spleen. The Peyer's patches are swollen and ulcerated. No growth is found in other organs except sometimes in the lungs. Dogs are unaffected. It cannot be certainly said whether the human body would possess any immunity. Two other species of mucor, M. pusillus and M. ramosus, have been found by Lindt to produce the same morbid changes in rabbits, the organs affected being, as in the other case, kidneys, intestine, mesenteric glands, spleen, and with an intensity repesented by the order of enumeration.

Pathogenic Fungi of the Human Skin.—*Trichophyton tonsurans.* This fungus, the cause of ringworm or tinea tonsurans of the scalp, tinea circinata of the skin, and tinea sycosis of the beard, is most nearly allied to the common moulds, but differs in having a much simpler structure. Its mycelium consists of ramified and distinctly septate hyphæ, varying in size, of which the average diameter may be taken as 6–7μ. When stained with methylene-blue, a central portion

FIG. 114.



Trichophyton tonsurans, from a case of tinea of the nails. Ramified septate mycelium, stained with methylene-blue. × 400.

which takes the color more deeply, is readily distinguished from a less intensely colored sheath. After growing for a certain time as mycelium merely, the ends of the hyphæ break up into spherical cells, which separated by fission or "abstriction" constitute the conidia, generally, but less accurately, called spores. They look rather polygonal with a high power. These are usually about the same diameter as the hyphæ, or 6.5 μ on an average. An indication of this process is seen at one part of Fig. 114. The conidia lie in the same plane as the mycelium, and there are no ascending hyphæ, conidiophores, or other form of fructification.

It is not easy to say what circumstances determine the formation of conidia. Generally, when the fungus grows in epidermis, or the nails, the mycelial form preponderates. In the hairs of the head the conidia are so abundant that mycelium is sometimes seen with difficulty, but may by proper preparation be traced running down the shaft of the hair (see Fig. 115).

Cultivation Experiments.—This fungus has now been repeatedly grown out of the body by methods which will be described in speaking of bacteria. The result is to show that the trichophyton is a species distinct from any known free-living species of mould. It grows very slowly at ordinary air temperatures, but most freely at about 84° F.: which is probably about the temperature of exposed parts of the human skin. According to Eisenberg,[1] the characters of the cultivated fungus are as follows:

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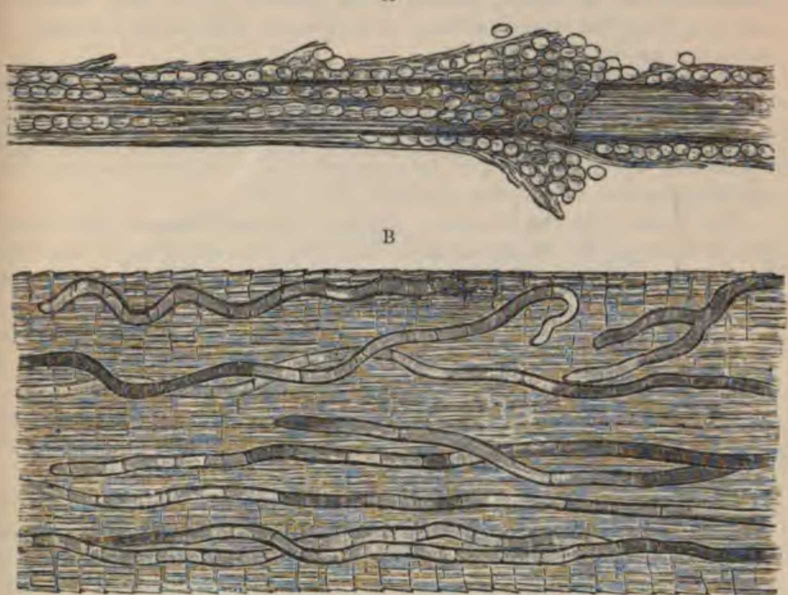
[1] Bakteriologische Diagnostik. Second edit. Hamburg und Leipzig. 1888. Dr Thin and Messrs. Morris and Henderson have made similar cultivations.

On gelatine it forms at 84° F. white masses or colonies with a prominent centre from which mycelium radiates outward. It rapidly liquefies the gelatine, and then the fungus floats on the surface as a thick scum, white above and yellow beneath. The growth succeeds best on blood-serum, the surface of which it covers with a film. After some days it turns yellow and liquefies the serum. The mycelium breaks up into spherical conidia just as in the natural growth. No other form of fructification is ever observed. The fungus thus cultivated has been inoculated into the human skin, and produces typical rings of Tinea circinata (Herpes circinatus).

FIG. 115.



Trichophyton tonsurans (after BRISTOWE).
A, fine hair from trunk, showing chains of conidia. B, hair from head, showing mycelium. × 500.

From the above characters both of the natural and cultivated fungus it appears that it differs widely from the natural forms such as Aspergillus, Penicillium, or Mucor. Its botanical relation to these forms must be left to botanists to determine.

Pathological Relations.—The trichophyton grows on the human skin, where the mycelium makes its way between the epidermic scales, causing them to desquamate or raising them up in the form of vesicles. By outward growth from a centre a ring is formed. The amount of inflammation produced varies in different cases; sometimes a vesicular, sometimes a pustular eruption resulting. This inflammation is, I believe, largely assisted by micrococci, which often accompany the fungus-growth—probably always when suppuration occurs—and I have often seen them in vesicles also. Perhaps the fungus prepares the soil for the growth of micrococci.

On the hairy scalp the mycelium also spreads in the epidermis, and when it reaches the hairs grows down inside the root-sheath, and also penetrates the hair-shaft, causing it to become brittle and break off. In this way the scaly patches of ringworm with broken stumps of hairs are produced.

The hairs of the beard may be affected in the same way, producing the disease called parasitic sycosis or tinea barbæ. In this form the fungus penetrates very deeply. Nails are affected in the same way as epidermis, the mycelium penetrating between the horny lamellæ, thus splitting up and destroying the nail (Fig. 114).

The identity of the fungus in the four forms of disease just enumerated is shown by numerous cases in which the contagion of one form has given rise to the others, as well as by the morphological identity of the parasite.

Similar affections of the skin are found in several domestic animals; and, in some cases at least, are caused by the same parasite. But it is possible there may be other species in certain cases.

Achorion Schoenleinii.—This fungus, the cause of the disease "favus" in man, as well as in mice, cats, and other animals, much resembles trichophyton.

The mycelium consists of hyphæ, which singly could not be distinguished from those of the fungus just described, but form very dense masses of a yellowish color and peculiar odor. When growing on the scalp it forms cup-shaped structures surrounding the hairs, which may be one-eighth to one-fourth of an inch across, and project to the same extent above the surface. By confluence of these, still larger masses result. On examination, this, the "favus" growth, is found to consist of a tangled mass of mycelium and conidia with fatty and granular matter. This production of conspicuous masses is the great distinction between the two parasites.

The achorion mycelium produces conidia precisely in the same way as the trichophyton.

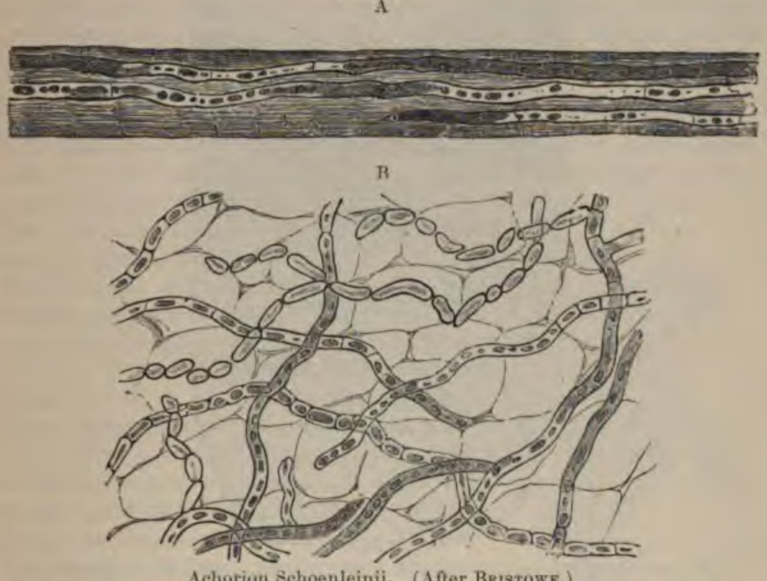
The conidia are sometimes said to be larger than those of trichophyton, and have been described as smaller (5.2 to 6.5 μ in diameter) and as being more oval. I have never been able to trace any constant difference in size, but the elements, both hyphæ and conidia of favus, generally look more distinct and brilliant than those of the other species, which, perhaps, arises from their having a higher refractive power; and the conidia are more regularly oval.

Cultivation Experiments.—The fungus of favus has been cultivated by the same method as that of ringworm. It grows very slowly on gelatine, producing white roundish colonies, liquefying the gelatine around them, but without forming conidia. On blood-serum at 84° F. it grows well, and produces oval conidia. At the ordinary air temperatures it not only ceases to grow, but absolutely perishes. This fact is of importance, as it may explain why favus is so little contagious.

being rarely transferred from one individual to another, so that cases commonly occur in an isolated manner.

The cultivated fungus has been inoculated into animals and men, and has produced typical cases of favus.

FIG. 116.



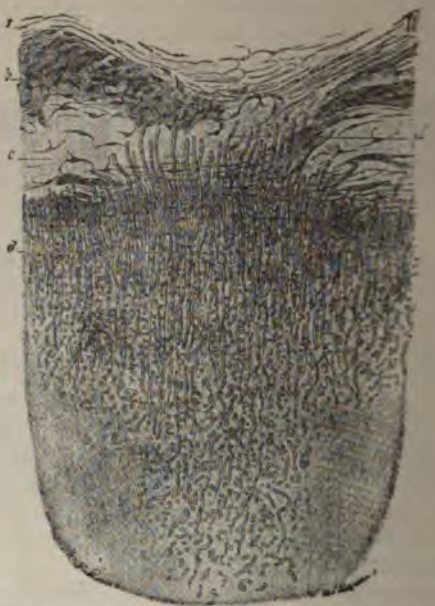
Achorion Schoenleinii. (After BRISTOWE.)
A, fine hair from trunk showing mycelium. B, mycelium and spores from neighborhood of a favus cup. × 500.

Pathological Relations.—On the bare skin the achorion produces at first appearances much like those of trichophyton, the mycelium penetrating between the epidermic scales and producing a ring of vesicles. But there is soon added to this the formation of the yellow favus cups and crusts, which result from the penetration of the fungus into the hair-sheaths; while the hair-shafts are also affected and break off. The fungus, however, grows much more deeply into the skin than the trichophyton (*see* Fig. 117). Hence ulceration and profound lesions of the skin may be produced.

It has often been suggested that favus and the different forms of ringworm may be produced by the same fungus with some difference of circumstances or constitution in the patient. But the details and experiments mentioned above make it quite clear that the one parasite always produces one kind of disease, and the other a different kind; while the differences in the mode of growth when cultivated, though slight, are constant. The clinical differences are also, at least in this country, where favus is so rare, quite conclusive, since no one has ever seen that disease give rise by contagion to ringworm, or *vice versa*.

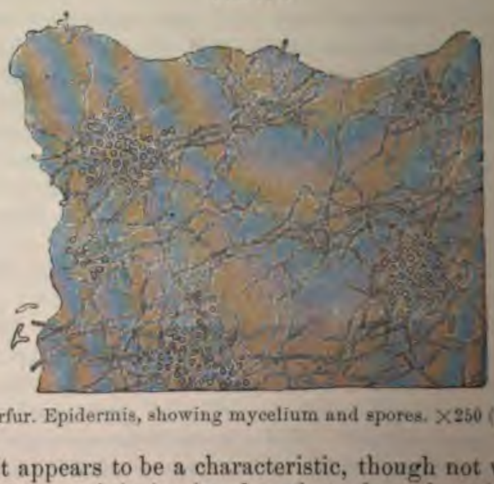
Isolated cases of favus are probably generally derived from d cats, or possibly from mice, from which animals cats the

Fig. 117.



Favus, showing penetration of skin by the fungus (Cornil and R
a, epidermis; *b*, *c*, corium; *d*, *d*, mycelium of fungus.

Fig. 118.



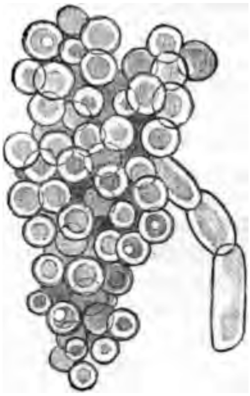
Microsporon furfur. Epidermis, showing mycelium and spores. ×250 (After B

acquire it. It appears to be a characteristic, though not very comm disease of mice; and it is singular that the odor given off fr favus-patches precisely recalls that of the familiar rodents. Th theory put forward by Grawitz that achorion and trichophyton are both forms of oïdium lactis, has been acknowledged to rest on an error.

Microsporon Furfur, the fungus of Pityriasis, or Tinea versicolor, differs considerably from those last mentioned. Its mycelium consists of ramified hyphæ, which show little definite structure, and produce conidia or spores at their free extremities. The process is, however, very different from that in the other skin-parasites. Instead of the hyphæ breaking up into conidia, a group of round spore-like bodies is produced by what looks like a process of budding.

The spores or conidia are in the same plane as the mycelium, and therefore the process is not like that of fructification in the aërial moulds; but if the spores were produced by an upstanding conidiophore the fungus would much resemble Penicillium. It has never been successfully cultivated in a perfectly pure state.

FIG. 119.



Microsporon furfur. Group of spores. × 1000. (After BRISTOWE.)

Pathological Relations.—The mycelium penetrates between epidermic scales, but not deeply, and conidia are formed in the same situation. There is no sign of inflammation, properly so-called, set up by the parasite, but the epidermis assumes a peculiar brown or fawn color, and slowly desquamates. It is transferable from one person to another, but only by somewhat close contact. Slight itching is produced.

This fungus shows a remarkable limitation in the parts of the body which it affects. It occurs on covered parts of the skin, especially the chest, abdomen, and shoulders, where it forms the well-known discolored patches known as Pityriasis versicolor. It may rarely spread to the neck, or, it is said, to the face. I have found it in two cases among scurf or dandruff from the head. It is never seen on the extremities. Warmth and a fatty condition of the skin, from sebaceous secretion, favor its growth. The natural history and botanical relations of the parasite must be regarded as quite unknown.

BLASTOMYCETÆ OR YEASTS.

These are distinguished from other forms of fungi by consisting of roundish or oval cells, which multiply by simple budding; a projection forming at one part of the cell which enlarges till it grows like the mother-cell and forms a separate cell, which either breaks off or remains attached in the form of a chain. There is no mycelium proper, though sometimes a tendency to form such a structure is observed; nor are there, generally speaking, any spores produced. But in artificial cultivations, spore-formation may be brought about by special conditions.

Some of the higher fungi (*e. g.*, mucor), as mentioned before, may, at one stage of their existence, pass through the form of yeasts. It is, therefore, possible that the plants now spoken of may be transitional forms of some higher fungi. But this is a botanical problem which need not be discussed here; since the forms are sufficiently constant to be recognized as distinct species. The chief physiological activity of yeasts consist in causing fermentation of sugar, that is, splitting it up into alcohol and carbonic acid.

The common beer yeast, *saccharomyces* (or torula) *cerevisiæ*, is the most important species, as being the chief cause of alcoholic fermentation. It consists of oval cells, measuring 8–9 μ in diameter, occurring either singly or in short chains.

Saccharomyces Ellipsoideus is the name given to the ferment of wine, which is constantly found in ripe fermenting fruits. Its cells are somewhat smaller than those of the last named species, measuring about 6 μ, and occur singly or in short chains.

Another species, S. *mycoderma*, which forms the scum on fermenting beers, and is also known as the vinegar plant, does not ferment sugar; and its supposed power of converting alcohol by oxidation into acetic acid appears to be doubted. It is mentioned here on account of its likeness to the chief parasitic yeast of the human body, now to be spoken of. The cells of S. mycoderma measure 6–7 μ long by 2–3 broad, and form long branched chains.

Saccharomyces Albicans is the parasite of thrush, the white patches often seen in the mouths of children, especially while fed on milk. It was formerly called oïdium albicans, and regarded as a mould-fungus allied to the oïdium lactis, which it must be said greatly to resemble. It is, however, most like the S. mycoderma, and has been regarded, though probably incorrectly, as identical with that fungus.

S. albicans consists of spherical or oval cells which remain united in long chains, and sometimes grow into threads which, however, are cylindrical cells, ten to twenty times as long as thick. The small cells are 3.5 to 5 μ in diameter. The fungus can be cultivated, and has some, though not much, power of fermenting sugar. It is said that it will produce the same diseases in fowls. Fowls, as well as sucking-calves, are subject to a spontaneous affection identical with that of the human infant. This fungus grows as a parasite upon the mucous surface of the mouth and sometimes of other parts of the alimentary canal. I have seen a great part of the ileum covered with a growth of the parasite, the surface over the Peyer's patches being singularly exempt. The case was that of an infant who died of atrophy. It is stated that the fungus has been known in one instance to pass into the circulation and cause embolism of the brain (E. Wagner); but in general it has no pathological results, except sometimes a slight amount of local inflammation; but even this is not often seen. Its fermentative action, if any, is exerted only on the contents of the digestive tract, not on the tissues.

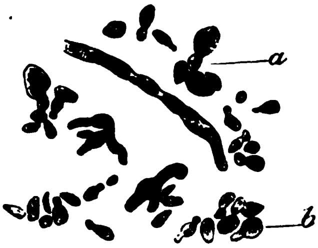
Parasitic Yeasts of the Skin.—It does not seem to be generally recognized that at least one, and possibly two, species of yeast-fungus are normally parasitic as epiphytes upon the skin.

Saccharomyces capillitii is very commonly met with in the midst of the scurf on the scalp, especially when this is abundant, in the condition called pityriasis (or Seborrhœa sicca of some authors).

It forms little oval cells, which appear to me to correspond precisely in size and form with the species called S. ellipsoideus from fermenting fruits, though I would not on that account say that it is the same species (Fig. 120, *b*).

In certain moist parts of the skin, more especially in the brown scaly patches on the inner side of the thigh called erythrasma, I have often seen a similar organism attaining a somewhat larger size, and sometimes growing into longer chains (Fig. 120, *a*). Whether this is the same species as that of the scalp or not, I cannot positively say. I have cultivated it so far as to get a large multiplication of the cells, which were in the cultivation more spherical, but not with sufficient success to form any positive opinion.

FIG. 120



Saccharomyces of the human skin. *a*, larger, perhaps distinct, form from moist skin; *b*, common form from the scalp. × 700.

Bizzozero has described two species of saccharomyces from the skin as S. ovalis and S. sphericus, which appear to agree with these two forms. Other observers (Oudeman and Pekelharing) have cultivated them and arrived at the conclusion that they are one species. Lutz has made some similar observations.[1]

Without deciding the question whether these organisms represent one or two species, it is interesting to inquire whether they exert any effect on the skin, or whether they merely live as saprophytes in the dead epidermic scales. Considering how often they are found in scaly conditions, and in numbers proportionate to the amount of desquamation, I am led to believe that these fungi are instrumental in causing overgrowth and desquamation of epidermis. It is possible that this may not be a morbid process, but a normal means of loosening the dead epidermis-scales, and thus, in a moderate degree, beneficial. At all events it seems a mistake to speak of these parasites as merely accidentally present, since they certainly grow and multiply on the scalp; and probably if too numerous are actually the cause of the pityriasis or dandriff. It has been thought that they are also the cause of falling of the hair, and thus of partial alopecia; a theory which seems to require further demonstration.

On the whole it seems that the yeasts have little, if any, pathogenic effect, and this might be expected from the fact that their fermentative action appears to be exerted only on vegetable substances, such as sugar.

ACTINOMYCES OR RAY-FUNGUS.

A remarkable form of parasitic plant, the botanical position of which is still uncertain, is recognized as producing the disease called

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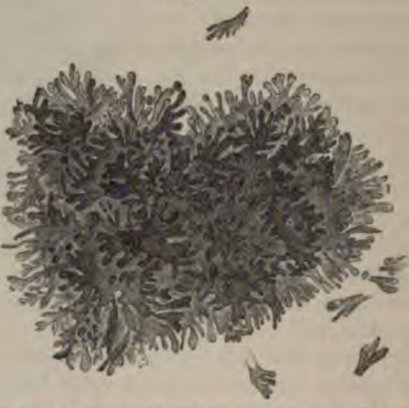
[1] See Baumgarten's Jahresbericht über Mikroörganismen for 1886, p. 338.

Actinomycosis in man and other animals. It is known as Actinomyces or Ray-fungus, and grows in roundish masses varying in size from grains just visible to those as large as a hempseed, of a yellow color

FIG. 121.



Actinomyces, from a case of disease in man. (Prepared by DR. ACLAND from a specimen of DR. ISRAEL'S.)

and granular surface. On microscopical examination these lumps have the appearance represented in Fig. 121, being composed of a number of radiating threads with swollen, club-shaped ends, forming a sort of rosette. Some fragments broken off are also represented. In some specimens narrow threads like hyphæ are seen forming coils in the central parts, or in one or two instances growing peripherally out of the mass. These threads have been supposed to be the mycelium of a mould-fungus, but are probably rather a form of leptothrix or cladothrix belonging to the schizomycetes which will be spoken of afterward. It has also been thought that they represent a different organism to the club-shaped rays. But recent researches tend to show that these threads are the living part of the plant, while the rays are degenerated or involutionary forms. The latter are often calcified.

Cultivation Experiments.—Boström has succeeded in cultivating the fungus from the central coils of threads, the rays remaining sterile. By special methods of cultivation a fungus was obtained agreeing in all essential particulars with the actinomyces of human and bovine disease, showing long threads like leptothrix or cladothrix, micrococcus forms, and, under certain circumstances, the club-shaped rays. It was inoculated into several animals, with the result of reproducing the original disease.

Actinomycosis.—The remarkable disease produced by this fungus was first observed in cattle, and afterward in mankind. In cattle it most commonly begins in the mouth in the form of tumors of the jaws and hard masses in the tongue, producing the so-called "woody tongue," and passing inward gives rise to large tumors in bones and internal organs, which before their real natu[illegible]overed were described under various names, such as lymphoma, sarcoma, osteosarcoma, etc. The characters of these tumors in animals are thus described by Johnne. They consist of a variable number of lumps or nodules varying in size from a hemp-seed to a pea, which are imbedded in a connective-tissue stroma. On section the imbedded nodules are seen to be yellowish granular masses, most of which are softened and surrounded by purulent or creamy fluid. The softened masses are easily pressed out, and then the tumor shows a honeycombed or spongy structure which is very characteristic. The imbedded nodules, when not softened, are found to show the structure of a typical tubercle with giant cells, epithelioid cells, leucocytes, and fibroid tissue, the actinomyces fungus acting as the centre of irritation. Except for the presence of this fungus, there would be, according to Johnne, no difference between the nodules and tubercles—a fact which confirms the explanation of the origin of tubercle, formerly given (p. 366). The mass does not, however, undergo caseous degeneration as a whole, but rather tends to suppuration. The actinomyces body often becomes calcified.

The disease is commonest in horned cattle, but may rarely affect swine and horses. The carnivora appear to be exempt.

Actinomycosis in man is a rare disease, not more than forty or fifty cases being known, and in this country very few have been recorded. The first undoubted cases were observed by Drs. Acland and Sharkey and Mr. Shattock in St. Thomas's Hospital, affecting the liver. In one instance an old museum specimen described as scrofulous disease was proved by Mr. Shattock to belong to this affection.

The tendency of the morbid products in man is to suppuration rather than tumor-formation; large abscesses, or else foci of suppuration in a spongy, honeycombed structure, being produced in the liver, and diffuse burrowing suppuration in other parts, such as the jaws, in the thoracic walls, and in front of the vertebræ, or in the mediastinum. Solid tumors, like those of cattle, have rarely been observed, but smaller masses of tubercular appearance are often seen in the liver.

According to James Israel, there are three ways in which the fungus may enter the body: (1) By the mouth, first lodging in some such place as a carious tooth or the crypts of the tonsils, and then passing into the alimentary canal or into the bones of the jaws; (2) By the respiratory tract, finding a lodgement on the bronchial mucous membrane or in the lung-tissue, and spreading to the pleura and surrounding connective-tissue; (3) By the intestinal tract, producing superficial lesions, and extending to the peritoneum and abdominal [illegible] by mestastasis to the liver. In some cases the channel [illegible] fungus has entered the body cannot be traced. Israel [illegible], that food is probably in all cases the original source [illegible] the fungus being contained in grain or other vege[illegible] He suggests that possibly some of the [illegible] (see chapter on Bacteria [illegible] [illegible]. Soltmann has [illegible] tally swallowed, which [illegible] luced either a [illegible] tion round the vertebral column and other parts. Even the lungs may be, as Israel suggests, infected through food, by aspiration of infective material from the mouth into the air-passages.

All the cases at present observed in this country in the human subject have been abscesses of the liver, which have a peculiar honeycombed appearance usually distinguishing them from other abscesses. The only proof, however, of the real nature of the disease is the discovery of the antinomyces-granules above described. In solid tissue these are easily seen, but their discovery in pus may be a matter of some difficulty. The resemblance of the smaller masses to tubercle is so great that some have doubted the mycotic character of the disease, and even the organic nature of the radiated bodies. But further researches have sufficiently established these points.[1]

Madura-foot or Mycetoma.—This disease, the "fungus-foot of India," is a remarkable instance of the fungus growing in the tissues of the human body. It may be defined as a diseased condition of the hands and feet, characterized by enlargement and distortion, due to thickening of the skin, with degeneration and caries of the bones leading to the formation of sinuses. From these sinuses are discharged certain roundish concretions, which in one form of the disease are yellowish and as large as millet seeds, in another form are dark brown or black and like grains of gunpowder. The black, but not the yellow, bodies are found to consist of a fungus-growth, forming a regular mycelium and black masses which have been compared to the truffle fungus. This parasite, called *Chionyphe Carteri*, has been generally regarded as the cause of the disease; but Messrs. Lewis and Cunningham think that it is merely a parasite of the kind which we call saprophytes, growing in the necrotic tissues. If this be so, the actual cause of the disease, which is confined to India, is quite unknown.

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[1] See J. Harley, "On a case of so-called Antinomycosis of the Liver," Medico-Chirurgical Transactions, vol. lxix. p. 135; and Proceedings Med.-Chir. Society New Series, vol. ii. p. 25; S. G. Shattock, Trans. Path. Society, vol. xxxvi. p. 254; T. D. Acland, Trans Path. Soc., vol. xxxvii. p. 546. For fuller accounts see James Israel, Klinische Beiträge zur Kenntniss der Actinomykose des Menschen, Berlin. 1885.

CHAPTER XLVI.

GENERAL ACCOUNT OF SCHIZOMYCETES.

THE most important class of plants which live as parasites in the human body, are the *schizomycetes*, or fission-fungi, sometimes called collectively "bacteria."

Schizomycetes are very minute uni-cellular plants, containing no chlorophyll (and thus commonly distinguished from algæ), which multiply by fission, or simply division, as well as, in some species, by spore-formation. Some produce spores in their interior, and in some the elementary cell itself becomes converted into a spore. These spores possess greater powers of resistance and stronger vitality than the plants themselves, so that the continuance of the species is effected by them, from one season to another, in conditions where the plant is unable to grow. They are hence called "resting spores." The substance of bacteria is an albuminous material called "mycoprotein" by Nencki. The outer, condensed portions of their body forming a membrane, contain also a cellulose. This membrane possesses great power of resistance to the action of acids and alkalies. The forms of these organisms are spherical, rod-like, or spiral. They sometimes grow out into long, jointed threads, and are occasionally united in colonies in which the individual cells are united by a transparent jelly.

Specific Differences.—With regard to these forms the important question arises, whether they are distinct species, or whether one species is capable of existing in several different forms. This has been a controverted question for a great many years, and is by no means easy of solution. If we examine, for instance, a putrefying liquid we may find at one time a great abundance of rod-shaped organisms (Bacterium termo); at another time we may find in the same liquid spherical forms or micrococci, and at another time rods differing from those first seen. It may accordingly be supposed that these forms are developed, one out of the other, being successive phases in the growth of one plant. On the other hand, it is possible that all these forms may be different species which grow successively in the liquid, all being present from the first; and that they replace one another either because the nutritive material suitable for the first is exhausted, or because the second is more successful in feeding itself and starves the first, or again because germs of another kind have obtained entrance in the meantime and have a stronger vitality than those originally present. Either of these explanations might be plausible and each has been proven to be true in certain cases. Certain bacteria have been clearly shown to pass through different phases of existence as micrococci, short rods, long rods, and colonies. This was proved by Ray Lankester, in 1873, for his Bacterium rubescens, since called Beggiatoa roseo-persicina and by Lister for Bacterium lactis.[1] On the other hand in putrefying fluids the forms successively observed are certainly in most cases of different kinds. Moreover, it has been clearly shown that many microörganisms maintain the same form and characters through many generations and under different circumstances.

The conclusion is that some species exist in one form only: while others pass through several developmental forms. The former are called monomorphic and the latter pleomorphic. To which class each species belongs can only be determined by observation and experiment: and with regard to many it is still uncertain to which they belong. The microörganisms which produce disease are for the most part, so far as at present known, either monomorphic, or show only a limited range of development. It should be borne in mind that the pleomorphism of certain species by no means implies the possibility of changing one into another. There is every reason to believe that the organisms of specific diseases are as constant in their specific character as we know the diseases themselves to be.

Distribution.—The schizomycetes are more widely diffused in nature than any other plants or animals, even more so than the mould-fungi. All natural water contains them, or their spores, and they may be found on all surfaces exposed to the air. No space, except one artificially produced, is free from them. This is shown by the fact that a drop of any kind of water (even distilled, according to Klein), or any fragment of substance which has been exposed to the air, will set up a growth of bacteria, if placed in suitable conditions; they, therefore, spring up everywhere, provided that the conditions of growth are present. The conditions of growth appear to be mainly two, namely, moisture and the presence of some nitrogenous material which serves as their food: for bacteria, unlike most of the higher plants, do not build up their tissue out of simply mineral substances, but for this purpose split up or decompose organic or at least complex materials. A certain range of temperature is also necessary. They cannot grow under freezing-point, though they may retain their vitality, and all species appear to be killed by a temperature of about 60° C. The spores of some species are, however, not destroyed by heating to boiling-point, but require a temperature of 120° or 130° to kill them completely. Most of the bacteria of disease will only grow at a temperature equal to, or approaching, that of the human body.

The part which bacteria play in nature is very important. Certain species live in dead organic matter, and are the direct cause of putrefaction. By their action the dead bodies of animals and plants are resolved into substances which can be incorporated with the soil, water, or air. Without them the earth would be encumbered with dead carcasses. Other species are the direct cause of the fertility of soils by converting ammoniacal substances into nitrates which are absorbed by plants. Other bacteria are the cause of many changes called fermentations, by which complex organic substances are split up into simpler chemical combinations. Looking at the effects produced by bacteria out of the body, it seems by no means surprising that if any species are capable of living within the body they should produce very important changes there.

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[1] Lankester's observations were the first which definitely established the genetic connection of several forms which were then regarded as distinct species. (Quarterly Journal Microsc. Science, N.S., vol. xiii. p. 408.)

The nature of the chemical processes set up by bacteria in albuminous matters is very significant. In putrefaction certain substances called ptomaïnes are produced, which have great resemblance to vegetable alkaloids, and, like some of them, are poisonous. Similar substances have actually been found to be formed in the living body in certain inflammations. We see, then, that the action of bacteria in the body will not only be to cause active tissue-change, but to produce injurious or toxic substances. Besides the toxic alkaloids or ptomaïnes, which are *functional* poisons, we must conclude that bacteria produce ferment-like substances, which act as *tissue poisons*, but the separation of them from the organisms producing them is very difficult. (*See* Chapters XXXI. and XXXII.)

The phenomena of specific infective diseases have for a long time been compared to fermentation, and the term zymotic or fermentative diseases, now used in official returns, expresses this analogy. This comparison must not be pressed too closely, for by fermentation we understand certain definite chemical decompositions, and the chemical changes which occur in disease are, from the number of substances which can be acted upon, very numerous and complex. But the analogy between the chemical changes which occur in disease and fermentations is clear.

Bacteria which do not Produce Disease.—Before speaking of the bacteria which actually produce disease, it will be well to say a few words about these other forms, which may in some cases be associated with the human body, but are not pathogenic.

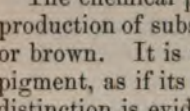
The bacteria which set up putrefaction may be distinguished as *saprogenic* or *septic*. There are probably many species which act thus. The best known form, called Bacterium termo, is not now recognized as one distinct species, but probably covers several species. Among those which have been cultivated are species of the genus Proteus (Hauser), which will be described farther on; but there is still some uncertainty as to the precise organisms concerned. The results of the chemical activity of septic organisms have already been spoken of.

Another group of bacteria live in organic liquids or solids, as milk, cheese, butter, bread, and produce certain chemical changes, consisting in splitting up complex into simpler combinations. These changes are called fermentations. Examples are the production of vinegar from sugar by Bacterium aceti; of lactic acid from milk by Bacterium lactis; of ammonia from urine by Micrococcus ureæ; and of butyric acid by Bacillus butyricus (*see* Fig. 127). Similar processes are set up by the growth of certain mould-fungi, as in alcoholic fermentation. The distinction from putrefaction is not always clear; but the name fermentation is given when the chemical decomposition is simple and definite, not complex. These bacteria are called *zymogenic* or fermentative.

The chemical processes set up by certain other bacteria result in the production of substances having a conspicuous color—red, blue, green or brown. It is the custom to call such a brightly colored substance a pigment, as if its functions were to give color to other things; but the distinction is evidently an artificial one, since we do not know that the optical property called color is necessarily connected with any other properties, physical, chemical, or physiological. Nevertheless, as a convenient label to put upon certain species which produce colored substances, they are called *chromogenic*.

Examples are the well-known Micrococcus prodigiosus, producing the phenomenon, once thought so mysterious, called red snow; the bacterium of blue pus (B. pyocyaneus) sometimes seen on surgical dressings (see Fig. 122); a peculiar form, Bacillus cyanogenus, apparently somewhat common in Germany, which gives a blue color to milk. Other rare forms have been found in water and elsewhere, such as Bacterium rubescens of Lankester, Micrococcus indicus of Koch, and others, which are cultivated in bacteriological laboratories.

FIG. 122.



Bacillus pyocyaneus (FLÜGGE). × 700.

Bacteria in the Human Body.—We will now consider what relations the groups above mentioned have to the human body.

The septic bacteria have been thought to be the cause of various diseases; but it is now known that most of them cannot live in healthy blood or tissues, being soon destroyed if they are introduced.

They may, however, live in dead, that is, gangrenous parts, and sometimes in the products of disease. Gangrene is, in fact, the putrefaction of a part still attached to the body, and is subject to the same laws as other putrefactions. Disease may be produced if the products of this process are absorbed; but, generally speaking, the conservative processes which are set up prevent this. Masses of dead tissue, the result of accident or disease, are liable to similar changes if the septic organisms once gain access to them. But if this be prevented by antiseptic methods, there are no bacteria and no putrefaction.

Pus or other morbid products, if retained, and in communication with the air, are very liable to harbor septic bacteria, as we see in the case of pus-cavities in the lungs or dilated bronchi, the contents of which soon become putrid. The same is the case with neglected wounds or abscesses.

It is, however, true that certain bacteria have been found in foul water or in putrid substances which have been shown by Koch to produce special diseases when inoculated into animals. But these appear to be special forms, only some few among the numerous species of putrefactive bacteria, and each of them affects only one distinct species of animals.

In the *intestinal tract*, a large number of bacteria of different species are often found, and this fact has been used as an argument against the pathogenic importance of bacteria. But to be in the intestinal canal and to be in the tissues are very different things. Man is, it should be remembered, a hollow animal; it is only when something has passed from the intestinal cavity into the tissues that it can be said to be, strictly speaking, *in* the body. But although it is very probable, if not certain, that chemical products resulting from the action of bacteria may be absorbed, there is no proof that the bacteria themselves pass in. Either the intestinal walls are, like the epidermis, impervious to them, or else they are at once destroyed on entering the blood.

In the stomach we find the *Sarcina ventriculi*, now regarded as a micrococcus, having a peculiar arrangement in bundles of four. It is found in healthy and diseased states, much more abundantly in the latter, but, so far as we know, does no harm. In small intestines many bacterial forms are found, which live upon and affect the food, not the tissues; probably assisting the processes of digestion by a sort of fermentative action. In the large intestine putrefactive bacteria are abundant, and doubtless have a large share in producing, by putrefactive changes, the special chemical constituents of the feces.

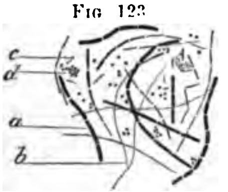
It has been found by Escherich that the meconium of infants which have not breathed is entirely free from bacteria, but that microörganisms appear in the excreta before food is taken—in some cases four hours, in others not till eighteen hours after birth. They appear to be introduced with the air which is drawn by infants into the œsophagus by swallowing and sucking movements. After twenty-four hours they increase in number and several species appear. On a pure milk diet two species predominate so much as to appear as if they were the only organisms present, viz., Bacillus coli communis and, in less number, Bacterium lactis aërogenis. The latter decomposes the sugar of milk. A quite different species, called Bacillus putrificus coli, is found constantly in other feces, but wanting in that of infants fed only on mother's milk (Bienstock). These facts show that the bacteria of the intestines are related only to the intestinal contents, and are pure saprophytes. In the rabbit's intestine bacteria penetrate normally into the lymphatic follicles, especially of the vermiform appendix, but not into the deeper parts of the intestinal walls, in healthy conditions.

If, however, the mucous membrane be deficient and ulcerated, these bacteria may penetrate the intestinal wall, and even be carried to the lymph-glands, though this is no proof that they caused the disease which produced the ulceration.

The mouth is inhabited by several microörganisms. Spirochæte plicatilis, in the form of long threads, occurs in the tartar of the teeth. A vibrio, resembling the comma-bacillus, has been found by Lewis in healthy persons. Another comma-bacillus or vibrio has been found in connection with caries of teeth, though it is not clear that it is the cause. Miller has isolated no less than twenty-five different species of bacteria from the mouth. The form most often seen is usually called leptothrix buccalis; but it is clear that this name covers more than one species (see Fig. 123).

In the *respiratory tract* many microörganisms are found which do not, so far as we know, produce any disease, but live in the dead epithelial cells, mucus, or morbid products of the mucous surfaces. They are often seen in sputum, and can be distinguished by reagents from the pathogenic organisms, especially the tubercle-bacilli, which occur there in diseased conditions of the lungs or air-passages. They are either micrococci or, in cases of putrid expectoration, septic bacteria.

FIG. 123.



Bacteria from the mouth. *a*, long threads usually called leptothrix buccalis; *b*, finer threads; *c*, bacilli; *d*, micrococci; × 600.

In the nose micrococci are found normally, and especially in cases of ozæna, where the organisms doubtless cause the putrid decomposition of mucus, etc., but are not shown to be the original cause of the disease.

Urine, when retained by paralysis of the bladder from spinal disease or stricture, very often contains organisms—usually the Micrococcus ureæ, which produces ammoniacal fermentation; hence the alkalinity of the urine. But it is doubtful whether this occurs except when a catheter has been introduced. Other bacteria, apparently septic forms, sometimes occur in the urine as it is passed ("bacteruria"); but, in the cases I have seen, without producing any bad results except rapid decomposition of the urine when passed.

Many bacteria may be found in the skin, but there is, in general, not sufficient moisture for them to develop except in moist parts, such as the axillæ and flexures of the thighs, or between the toes.

Micrococci are the commonest forms. A bacterium capable of growing into threads has been observed in the disease called erythrasma, but its true nature is still uncertain.

Micrococci have been described as occurring in dead hairs or scurf; and dead epidermic scales often contain them. But since these are found in all dead and decaying matters, it has yet to be proved that they are the cause of disease.

All the above-mentioned species, though many of them may fairly be called parasites in the same sense as intestinal worms, grow as saprophytes, living upon the waste materials of the body, and, so far as is known, producing no disease in man. Some of them, however, are decidedly pathogenic for other animals if artificially introduced into their bodies.

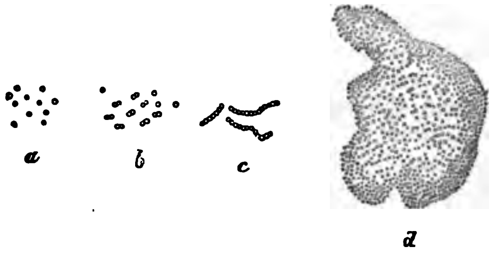
Another very important question arises, whether the living tissues and blood of healthy persons under ordinary circumstances contain bacteria; for it is evident that if it were so, serious errors of observation might result. Many researches have been made to investigate this point, and the verdict of the great majority of experimenters, notwithstanding the discordant results obtained by others, is distinctly in the negative. Lister and Cheyne in this country have arrived at this conclusion, agreeing with those of several German pathologists, though differing from those of Horsley, Zweifel, Tiegel, and others. Recently very careful researches have been made by Ballance and Shattock to test the question whether healthy tissues contain bacteria or germs susceptible of artificial cultivation. Pieces of tissue, and also of new-growths, were placed in the incubator and kept for some days or weeks at a high temperature; but in no case did any growth of organisms result, except in pieces of liver, an organ which, from its proximity to the alimentary canal, would be more likely than others to contain saprophytic bacteria.[1] On the other hand, it has been often shown that septic bacteria soon die if introduced into healthy blood or tissues; though, according to Wysskowitsch, certain species may remain for some days inactive, though capable of growth, in certain organs, especially the liver and spleen.

CLASSIFICATION OF SCHIZOMYCETES.

This question, so interesting as a part of natural history, must here be regarded only from the point of view of practical utility. Two systems have obtained considerable popularity, that of Cohn and that of Zopf. The former is based upon the supposition of the constancy of forms, the latter gives more weight to their mutability. We shall adopt, with some changes, that given by Hueppe, which is modified from Cohn's.[2]

The first requisite in classification is to have precise names to designate the *forms* which are met with. This may be done without deciding the question how far these forms are changeable into one another, or how far they represent true species.

FIG. 124.



Micrococci in various modes of growth (FLÜGGE). × 700. *a*, micrococcus; *b*, diplococcus; *c*, streptococcus: *d*, zooglœa.

Forms of Bacteria.—The simple forms here represented must be regarded as single cells. If united in various ways they produce compound forms.

A. Single-celled forms.—These are unicellular and multiply by fission.

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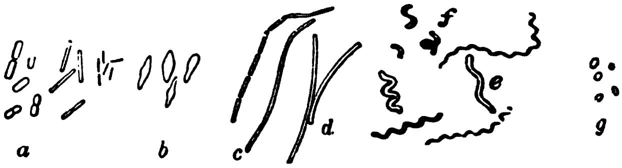
[1] Transactions Pathol. Society, xxxviii. 412.

[2] Die Methoden der Bakterienforschung, 3d ed., 1886. De Formen der Bakterien, 1886.

a. Cocci, or micrococci, forms, spherical or slightly ovoid (Fig. 124, *a*).

b. Rods in which one axis is much longer than the other. If the sides are curved, a spindle-shaped rod is produced (Fig. 125, *b*); if the sides are parallel, a straight staff (Fig. 125, *c*, *d*). If the ends are rounded, it will approach an ovoid (Fig. 125, *a*). The length of rods is very variable, so that the distinction of short rods (as bacterium) and longer rods (as bacillus) is comparatively unimportant. They often appear spherical if of small size and seen endways.

FIG. 125.



Forms of bacteria (FLÜGGE). × 700.

a, bacillus; *b*, clostridium; *c*, threads and apparent threads; *d*, false ramifications; *e*, vibrio; *f*, spirillum; *g*, spirochæte; *h*, spores.

c. Spirals or cork-screw forms, apparently curved, but really spirally wound rods, which are two to four times as long as broad. These have lately become known as "comma-bacilli." The degree of curvature or spiral winding varies according to external conditions and the stage of division, and rapidly alters if the cell is flexible. Curved or spiral rods may easily appear straight, if seen in particular directions.

Flagella or cilia are seen in some bacteria.

d. Degenerative forms.—If bacteria die and undergo granular degeneration, they may show irregular forms.

B. **Combinations of Single Cells.**—*a.* If growth takes place in one direction only, a chain of cells is formed, which, when the cells are distinct, is the *rosary* form (*c*, in Fig. 124). If the chains are composed of cylindrical segments less clearly separated, the appearance of a thread is produced (*c*, in Fig. 125), and such chains are with difficulty distinguished from true homogeneous threads. By the union of spirally curved elements, spiral or corkscrew threads are produced (Fig. 125, *e*, *f*, *g*), and it is very difficult to say whether such threads are really made up of segments, or of one continuous piece.

b. Growth may take place in various directions in a plane, forming a flat mass or lamina;

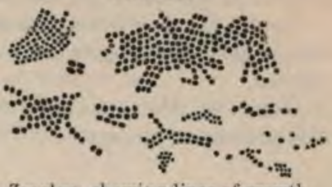
c. Or may extend in all three dimensions, forming solid masses, of which the type is *sarcina*.

d. The cells may form quite irregular masses or agglomerations.

C. **Colonies or Zoogloeæ.**—In the above-named forms the elements are distinct, without any intervening substance; but if they are connected together by an intercellular gelatinous substance, the form called zooglœa (or living jelly) is produced. Either cocci or rods may form a zooglœa; and sometimes different forms of elements are seen in the same.

The above-mentioned forms of growth do not of themselves constitute species or genera. Some species go through a cycle of forms, and one may be in turn a micrococcus, a bacillus, a leptothrix, etc. Others are known only in one form, and hence it is not certain that all species do not run through several forms, but probably the number of pleomorphic species will be increased as they are better known.

FIG. 126.



Zooglœa, showing lines of growth. × 800.

From a micrococcus growth on the hairs of the axilla.

To distinguish genera and species—*i. e.*, to make a classification, doubtless the best guide would be, as in other orders of plants, the *fructification*, but this is in many cases not known. This process is very simple in the schizomycetes, consisting merely in the formation of a "resting-spore." Such spores, when placed in favorable circumstances, by a simple process of germination, reproduce the bacterium. The germination of spores is seen in Fig. 127 D.

In those kinds which produce spores, two modes of formation are seen: (1) endogenous, where the spore is formed within the cell-membrane from the protoplasm. This is seen in the anthrax-bacillus. (2) External spore-formation, in which the cell itself, or one segment of a chain, becomes converted into a spore called arthrospore (joint-spore). Such a spore may be larger than the ordinary vegetative cells, but otherwise so much like it as to be with difficulty recognized. De Bary holds that in micrococci there is no distinction between specifically reproductive cells (or spores) and vegetative cells. These species in which no endogenous spore-formation is seen probably form arthrospores, or at least may be classified on this basis. Two divisions may be formed:

A. Bacteria forming *endogenous* spores, which may be called endosporal cocci or bacteria.

B. Bacteria forming *arthrospores*, or none, which may be called arthrococci or arthrobacteria.

In each of these divisions, cocci-forms, straight rods, and spirals occur, so that it will be most convenient to take the elementary forms separately, and use the reproductive classification only for making divisions in each group. We admit in all seven families: (1) arthrococcaceæ; (2) endosporal coccaceæ; (3) endosporal bacteriaceæ or bacilli; (4) arthrobacteriaceæ; (5) spirobacteriaceæ; (6) leptotricheæ; (7) cladotrocheæ.

Coccaceæ form two families, according as there are, or are not, endogenous spores.

FAMILY I. **Arthrococcaceæ.**—The ordinary (vegetative) cells have the form of cocci. The ordinary forms of so-called micrococci, with doubtful exceptions, belong to this class. **Genera are formed** according to their different modes of combination.

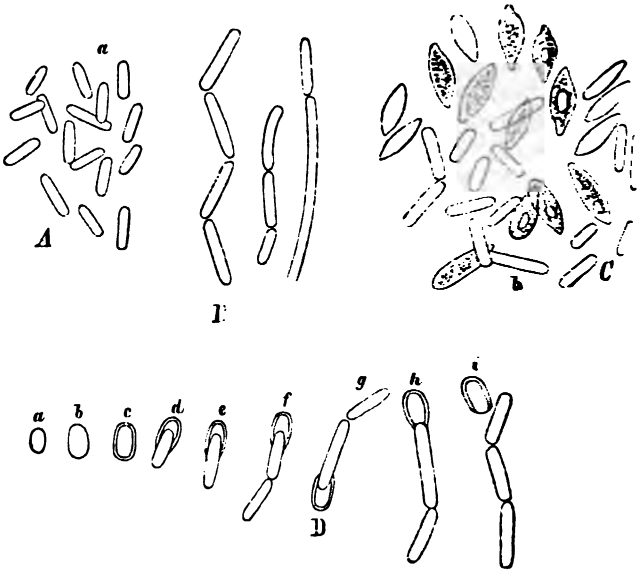
Genus 1. ***Streptococcus*** (chain-cocci).—The cells form chains (Fig. 124, C).

Genus 2. ***Merista*** or ***Merismopedia*** (plate-cocci).—The cells are united in two directions in one plane, forming plates; most typically in groups of four, *e. g.*, Gonococcus.

Genus 3. *Sarcina* (packet-cocci).—The cells divide in all three dimensions, forming solid masses like "bales," or packets, often cubical.

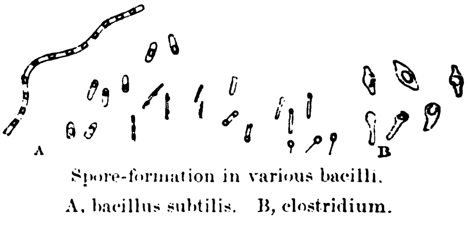
Genus 4. ***Micrococcus*** or ***Staphylococcus*** (mass-cocci) forming irregular masses or clumps.

FIG. 127.



Clostridium (bacillus butyricum) (after PRAZMOWSKI). × 1000. A, colony of bacillus. B, chains. C, bacilli becoming spindle-shaped and forming spores. D, germination of spores. a-i, successive stages.

FIG. 128.



Spore-formation in various bacilli.
A, bacillus subtilis. B, clostridium.

Genus 5. *Ascococcus* (pellicle-cocci).—The cocci united in gelatinous pellicles or spheroidal masses. Doubtfully distinct. The genus is not pathogenic.

FAMILY II. **Endosporal Coccaceæ** (forming endogenous spores).—The chief genus—Leuconostoc—is not pathogenic.

Bacteriaceæ form also groups, according as endogenous spores are present or absent.

FAMILY III. **Spore-forming Bacteriaceæ, or Bacilli.**—These are rods of all lengths, some so short as to be indistinguishable from micrococci. They may be united into threads, spiral or straight; or into irregular masses. They produce endogenous spores.

Genus 1. *Bacillus.* The rods do not alter their shape during the spore-formation, *e. g.*, B. subtilis and B. anthracis.

Genus 2. *Clostridium.* The rods are either always spindle-shaped or become altered in shape during spore-formation, *e. g.*, Clostridium butyricum (Fig. 127).

FAMILY IV. **Arthro-bacteriaceæ.**—The cells are rods or, according to some, cocci also. They may be united in a zooglœa or may form long threads. They form no endogenous spores, but in some cases *arthrospores.*

Genus 1. *Bacterium* (strictly so-called). This genus includes straight rods which form no spores.

Genus 2. *Proteus* (spirulina) shows great diversity of form—cocci, chains, rods, and threads. Motile in certain stages.

The spiral bacteria also show forms with and forms without endogenous spores.

FAMILY V. **Spiro-bacteriaceæ.**—Small curved rods, like fragments of a spiral, known as "comma-bacilli." They may unite to form corkscrew-like threads, which vary greatly in length and amount of curvature. Some form endogenous spores, some not.

Genus 1. *Vibrio.* The rods enlarge and spores are formed in the dilated part (Fig. 125, *f*).

Genus 2. *Spirillum.* Spores formed without any alteration in the shape of the rods in some genera which are not pathogenic. The pathogenic forms produce no spores, or else arthrospores. They include the "comma-bacilli" and the genus spirochæte. This genus might well be divided into two, as is done by Hueppe (Fig. 125, *e. g*).

Two other families, in which the chief form is that of long threads, are separated by Zopf. According to him, the threads differ from the long threads which result from the growth of bacilli. The families are:

FAMILY VI. **Leptotricheæ.**—In early stages appear as cocci or rods; later, thread forms, straight or spiral. The threads show a distinction between the base (where they are attached) and the fore end. This alone distinguishes them from the threads formed by bacillus, etc.

Genus 1. *Crenothrix* occurs in rods and threads, which are distinctly articulated, and show a sheath. According to some there are also cocci-forms.

Genus 2. *Leptothrix* shows the same variety of forms: threads articulated or inarticulated, without a sheath. One species of leptothrix occurs in the mouth, as already mentioned (Fig. 123).

FAMILY VII. **Cladotricheæ.**—Occurs in rods and sheathed threads, which may be undulated or spiral, and sometimes show a false ramification (*see* Fig. 125, *d*).

Genus, *Cladothrix.* Extremely common in water; one form has been found in the lachrymal canals of the human eye.

ANALYTICAL TABLE OF BACTERIA (HUEPPE).

Cocci; round or oval cells.	Arranged in chains			**Streptococcus.**
	" " fours or small chains			**Merista.**
	" " eight " "			**Sarcina.**
	" " irregular massess	Zooglœa various		**Micrococcus.**
		Zooglœa in spherical encapsulated mass.		**Ascococcus.**
Cells cylindrical; rods.	Longer or shorter threads without distinction of base or apex.	Threads straight or wavy; no endogenous spores		Arthrobacterium.
		Threads straight, wavy or spiral; motile; no endogenous spores		Proteus (spirulina).
		Threads straight or wavy: formation of endogenous spores.	without alteration of shape of rods	Bacillus.
			rods becoming spindle-shaped	Clostridium.
	Threads showing distinction of base and apex.	Threads without a sheath		Leptothrix.
		Threads with a sheath	not ramified	Crenothrix.
			ramified	Cladothrix.
Curved or spiral rods.	Spiral threads flexible or stiff.	Endogenous spores with alteration of shape		Vibrio.
		Endogenous spores or arthrospores, or none, without alteration of shape		Spirillum.

The above classification, it must be repeated, is one of forms only, and it is still uncertain how far these forms represent actual species. But in the meantime it is a great convenience that these forms should have names.

If we were only speaking of pathogenic bacteria, a simpler classification would suffice. It would be enough to recognize (with Flügge) four chief groups, viz., (1) micrococci; (2) bacilli; (3) spirilla; (4) bacteria, with variable forms of growth. The last group comprises species which may appear in simpler forms, but, as it includes no species pathogenic for the human body, we need not further consider this group here.

Relation of Bacteria to Oxygen.—Another important distinction based upon physiological activity may be drawn between those bacteria which require air, *i. e.*, oxygen, and those which do not. The first, called by Pasteur *aërobic*, can only live, or at least grow, where there is some access of air; the second class, *anaërobic*, only where air is excluded—that is, under the surface of the fluid or other nutritive medium. The latter are regarded by Pasteur as always exerting a fermentative action on the medium, which however, though generally, does not appear to be invariably the case. There are some organisms which are capable under certain circumstances of growing under both of these conditions.

Further Distinguishing Characters.—Since the forms of bacteria do not always furnish constant distinguishing characters, and, moreover, many apparently different species are identical in form, recourse is had to characters derived from the mode of growth in artificial cultivation. To explain this point a few words must be said about the methods of cultivating and isolating bacteria, though it will be impossible to give such details as are necessary for practical use.

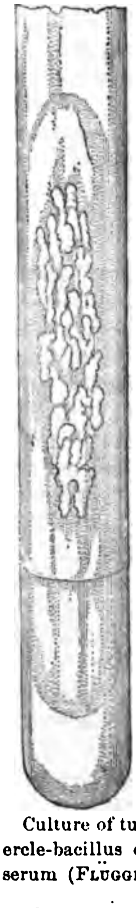
CULTIVATION OF BACTERIA.

Many naturalists have at various times attempted to grow bacteria under artificial conditions, and watch their development. Generally this was done in liquid media, which though they might allow of the growth of the organisms, did not make it possible strictly to isolate them, and thus different forms would get mingled together, and their true genetic relations become obscured. It is the great merit of Koch to have devised methods of growing these organisms in solid media, in which, like plants rooted in the soil, each growth remains isolated in one spot.

The medium most generally used for the purpose, nutrient gelatine, contains nutritive material in the form of peptonized meat-juice, prepared in a special way, and sufficient gelatine—from 5 to 10 per cent.—to make the mixture, which is prepared with the aid of heat, solidify on cooling. When solid it liquefies again if heated to about 85° F. It may be made alkaline with carbonate of soda (since some bacteria grow best in a slightly alkaline medium), and neutralized or rendered faintly acid, if necessary, with a trace of lactic acid.

For use it is liquefied and poured, with certain precautions, into test-tubes (which are filled up to one-third and then closed at the top with a pledget of cotton-wool), or under certain circumstances into other vessels. The gelatine medium has next to be sterilized; that is, heated so as to destroy any living bacteria or spores which may be present in it. This is not effected by a single boiling, but is best done by heating the tubes to boiling-point in a water-bath, during at least ten minutes daily for four or five days. One great advantage of gelatine media is their transparency, which permits the first beginnings of growth to be traced.

FIG. 129.



Culture of tubercle-bacillus on serum (FLÜGGE).

For certain purposes it is desirable to have a medium which will bear a higher temperature without liquefying, and for this purpose a vegetable jelly called agar-agar, derived from certain species of algæ and imported from Japan, is employed. It is added to peptonized meat-juice in the proportion of one or two per cent., and the mixture prepared as in the case of gelatine. The jelly thus prepared is solid up to temperatures of 100° or thereabouts, and quite as transparent as the gelatine.

There are certain organisms for which neither of the above mediums supplies a suitable soil, and for such Koch has introduced a method of cultivation on coagulated blood-serum. The serum is prepared from fresh blood, and, after careful sterilization by special methods, is solidified at a temperature of about 150° F., which operation is usually effected in a test-tube held obliquely, so that the coagulated mass has a sloping surface, on which the organism to be cultivated may be implanted. This medium is especially useful for the tubercle-bacillus.

Other solid media. For certain cultivations, the surface of a cut potato is very suitable soil. The outside of the potato is sterilized; it is steamed, and then cut in half with special precautions, with a sterilized knife. Being then carefully preserved from dust or other contamination, implantations of organisms can be made upon the cut surfaces, and give colonies or growths, often of characteristic appearance and color. Potato-paste, bread-paste, certain kinds of boiled vegetables and fruits, are sometimes used in the same way. White of egg is also occasionally used as a solid substratum.

Sterilization.—Before speaking of the precise method of making cultivations, it must be shown how such experiments can be secured against failure through the casual entrance of the organisms which are so widely distributed in the air and on all the solid objects necessarily made use of in these processes.

For knives, forceps, test-tubes, glasses, and all kinds of apparatus, the only effective means of sterilization is heating to a temperature considerably above boiling-point, and 300° F. is generally taken as the necessary minimum. Platinum wires, needles, and knives may be heated in an open flame (except for the drawback of destroying the temper of the steel); otherwise all such objects are heated in a "hot-air sterilizer," *i. e.*, an iron chamber heated by a gas flame, so regulated as to keep a uniform temperature of 300°. This apparatus is used for test-tubes, glasses, funnels, cotton-wool, and other miscellaneous objects, which should be exposed to the temperature mentioned for one hour.

All objects used must be sterilized immediately before an experiment, or else preserved by very special methods.

Liquids are sterilized by repeated boilings, as mentioned above, and such boilings may be carried on in chambers filled with steam, which preserves a temperature of 212° F.

Method of Cultivation.—The actual process of cultivation is somewhat as follows: A tube of nutrient gelatine (say) is taken for the first experiment. A platinum wire, either straight or bent into a small noose or eye (in German *öse*) is dipped in the fluid, such as water, blood, serum, etc.; or made to touch any soft material, such as mucus, in which the microörganism is contained, so as to bring away the smallest possible quantity. The tube is then inverted (to prevent germs from falling in from the air) whenever this is possible, and the wire is either made to touch, or dipped below the surface of the gelatine and withdrawn. In the case of solid substances or tissues, such as skin, a small portion is detached with a sharp needle or scalpel, and either placed upon or buried in the gelatine. A similar process, with certain obvious variations, applies to agar-agar or blood-serum tubes.

The tube is then either placed in the incubator or kept at ordinary temperatures, as the case may be. If the medium is suitable, and there be an organism present, after a longer or shorter time growth takes place, and will be shown by turbidity of the gelatine, or the formation of definite masses, either along the whole of the track of the needle, or at the surface only or in the deep parts. The forms of the objects thus produced often serve to distinguish different species, especially in combination with other characters, such as whether the gelatine is or is not liquefied by the growth, whether gas-bubbles are evolved or not, and so on. Other important features are the rapidity of the growth and the temperature at which growth takes place. In regard to the latter point three temperatures are important. The lowest at which the organism will grow, or its *minimum;* the highest, any increase over which kills the organisms, or the *maximum;* and, finally, that at which it grows most rapidly and vigorously, or the *optimum.*

By combining all these and similar characters, a specific distinction may often be drawn between organims which are morphologically quite indistinguishable; as may be seen in the cultivations of the cholera-bacillus and allied forms, figures of which are given farther on.

The most obvious difference between organisms is whether or no they liquefy the gelatine; and as regards non-parasitic bacteria, they may be, for the practical purposes of the laboratory, divided by this criterion into two main groups.

Plate-cultivations.—The above method of cultivation in single tubes may be sufficient if only one organism is present: but when there is a mixture, as is generally the case in the original specimens, they must be isolated and separated by the plate method, one of Koch's most ingenious inventions. It is as follows: The original specimen, or preferably, an original tube-cultivation, is introduced into a fresh tube of gelatine melted by heat, and is thoroughly mixed up with the gelatine by gentle movements of the tube. From this tube a small portion may, if necessary, be introduced into a second tube prepared in the same way, and thoroughly mixed so as to dilute the original contents; and the dilution may be carried still farther if desirable.

The contents of each of the tubes are then poured out separately upon a glass plate, about six inches by four, and after being carefully spread over it, allowed to cool and solidify. The plates are then placed under a bell-glass in a moist chamber, and the cultivations allowed to grow. The result is that the organisms present spring up at different parts of the plate in isolated cultivations, which may be distinguishable by their appearance, or recognized with more certainty under a low power of the microscope. Of these a small portion may be removed with a needle and examined separately, or made the starting-point of a new cultivation.

Other Methods of Cultivation.—Another method of plate-cultivation sometimes useful is to spread a single drop of gelatine on a glass slide, and allow it to solidify. Then the organism may be sown in streaks or lines, and its development watched under the microscope. But such specimens are with difficulty protected from impurities.

A more satisfactory method for microscopical observation is cultivation in the "hanging drop." It requires a glass slide with a hollow ground in it, so as to form a shallow cell. Over this is placed a cover-glass, on the under surface of which is a drop of nutrient liquid inoculated with a minimal quantity of the organism. The edges are made air-tight with a little vaseline, and a moist chamber is formed, accessible to observation from above even with high powers, in which the development of any organism may be watched from day to day. It is very suitable for moulds as well as for bacteria.

Liquid media are much used for certain cultivations. Broth, made from some kind of meat and carefully sterilized, is that most generally employed. Fresh serum and the liquid of serous effusions have been used, and sterilized milk is a good soil for some species. Cultivations in liquid are generally carried out on a small scale: as, for instance, in the hanging drop or in microscopical cells.

Some cultivations can be carried out at the ordinary temperature of a room, but others, and especially those of truly parasitic organisms, require a temperature approaching that of the human body. In order to satisfy these conditions, recourse is had to an apparatus called an incubator, or hot chamber furnished with a self-regulating gas-burner by which the temperature is kept constant. In such an apparatus cultivations can be carried on for weeks or months at any temperature that may be desired. For observations under the microscope some modification of the well-known warm stage is used.

Continued Cultivations.—When a growth is obtained consisting of one organism alone, or a "pure cultivation," a small portion may be transplanted on a fresh tube of gelatine, and so on through many generations. The advantage of this is that the organism is thus entirely separated from any portion of its original soil or other extraneous matter. Koch carried the cultivation of the tubercle-bacillus through thirty-four generations in nearly two years, and since then through a much longer series.

In many cases a better result is obtained by introducing the cultivated bacterium into the tissues or blood of a small animal, such as a mouse or guinea-pig. The animal body serves as a very perfect cultivation-apparatus of constant temperature, and if it is suited to the bacterium, the latter will multiply enormously. An inoculation from this animal may then be made into another, and so on through as many generations as may be desirable. By this means the identity of certain specific diseases has been established.

CHAPTER XLVII.

CONNECTION OF BACTERIA WITH DISEASE.

PATHOGENIC organisms not only live in the human body but are the cause of disease there. They often closely resemble non-pathogenic forms, but must not be considered as being the same organisms living under different conditions. All species which have been thoroughly investigated show some characters of form, or of functional activity, or mode of growth which distinguishes them. There is no proof of there being any transformations of innocent into pathogenic forms, though this has been supposed by Büchner and others, but the evidence for such a change has completely broken down.

We may indeed suppose, on Darwin's principles, that the pathogenic species have been evolved out of the others by a process of natural selection. But such changes require the long periods of time which alone make the transmutation of species conceivable. They are not effected in one generation. There is only the same general resemblance between certain parasitic forms and forms living free in nature, that there is between parasitic filariæ, for instance, and free filariæ living in water. We shall see too that, as in the case of parasitic animals, some of the bacteria are true parasites, some occasional and some pseudo-parasites.

In order to *prove* that a special microörganism is the cause of any disease, certain conditions have to be fulfilled, which have been clearly laid down by Koch.

1. The microörganisms must be constantly found in the blood or tissues, or both, of the men (or animals) suffering from the disease.
2. The microörganisms must be got to grow in some medium outside the body, and by successive cultivations completely separated from all matter belonging to the body from which they came.
3. After being thus cultivated through several generations, the organism must be inoculated into some animal, and reproduce in it the original disease.
4. In the tissue or blood of this animal the same microörganism must be found which was found in the original patient.

It is sometimes impossible that all these conditions should be fulfilled, since there are some human diseases which are not known to affect the lower animal and which cannot be communicated to them, so that inoculation experiments do not succeed.

This is the case with cholera, leprosy, and syphilis; or at least the results of inoculation of these diseases are ambiguous. In the meantime analogy with other cases, in which the evidence is complete, may give to the pathogenic character of such organisms the very highest degree of probability.

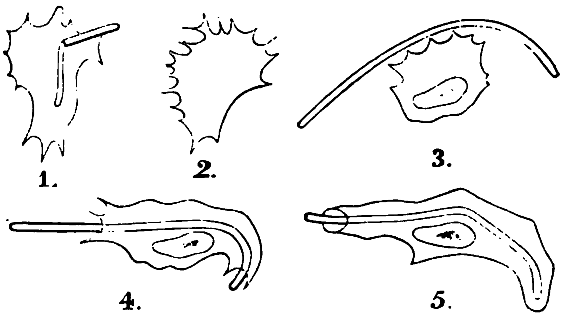
There are, again, some organisms constantly associated with certain diseases for which no suitable medium of cultivation has yet been found. The bacillus of leprosy is an instance.

When pathogenic organisms are introduced into the body, they give rise to two kinds of actions. The first are *local*, or tissue changes, consisting partly in destruction of certain elements, and from the reaction of the body upon them, partly in new growth. The second are *general*, being fever, cachexia, and the like, which may be fatal. The first kind of action is most conspicuous in what we have called the infective granulomata; the latter in the specific infective fevers; but often both are combined. Tubercle is the most perfect instance of a combination of local and general disturbance.

Tissue-changes.—The microörganisms specially attack cells, both migratory leucocytes and tissue cells.

The former may often be seen enclosing microörganisms in their substance. This phenomenon may be described in two ways. We may say that the bacteria penetrate the cells, or that the cells absorb the bacteria. This is a sort of struggle between the vitality of the two. If the virus be too strong for the cell, the latter dies; and hence we see that necrosis or tissue-death is a conspicuous phenomenon in all these diseases, and is never wholly absent. On the other hand the cell may, according to Metschnikoff, in some cases, get the upper hand, and either destroy the foreign organism by a process of intercellular digestion, or at least carry it away from the scene of action.

FIG. 130.



Leucocytes of frogs absorbing anthrax-bacilli.

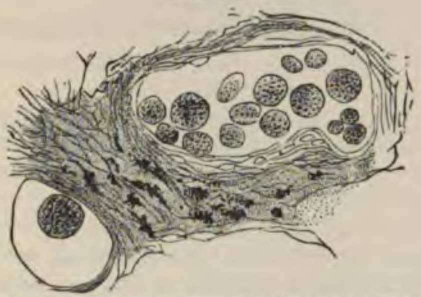
1, leucocyte with a bacillus half-enclosed in its protoplasm; 2, the same leucocyte ten minutes later, the bacillus having disappeared; 3, leucocyte attacking a bacillus; 4, the same a few minutes later, with the bacillus half-enclosed; 5, the same a few minutes later still (Metschnikoff, Virchow's Archiv, vol. xcvii., plate 16).

Metschnikoff found that, in frogs and other cold-blooded vertebrates which are immune against anthrax, the leucocytes, and especially the large cells which he calls phagocytes, absorbed and apparently destroyed anthrax-bacilli artificially introduced into their bodies (*see* Fig.

130). In rabbits and guinea-pigs, on the other hand, animals very susceptible of anthrax, the leucocytes did not appear to possess this power of dealing with the bacilli when injected into their blood. He supposes accordingly that the immunity of the first-mentioned class of animals is due to the bacilli being destroyed by the elements of the body. To test this supposition he introduced into rabbits and guinea-pigs anthrax-bacilli weakened by being heated to 42° C.; that is, a so-called "vaccine" of anthrax. These bacilli were found in many instances enclosed in, or absorbed by, the leucocytes near the spot where they were introduced. Further comparative experiments seemed to show that, after having dealt with the bacilli of the vaccine, the leucocytes of the warm-blooded animals acquired the power of destroying fresh bacilli of unimpaired virulence; but this conclusion was hardly established. Without questioning the reality of the action of the frog's cells on microörganisms, it must be said that the numerous experiments of Wyssokowitsch with other pathogenic bacteria have not confirmed these results as regards warm-blooded animals. Such a process was established only in the case of two or three specific microörganisms, and in these cases the cells appeared to be succumbing to the attacks of bacteria (*see* p. 93).

In this case the migratory leucocytes can do no more than carry the bacteria they have absorbed, as they do other foreign substances, such as granules of pigment, into the lymphatics, and thus to the nearest lymph-glands; and this is sometimes, though not always, observed (*see* Fig. 131).

FIG. 131.



Leucocytes carrying away pigment-granules (CORNIL and RANVIER). × 200.

From a section of lung in interstitial pneumonia. On the right hand an alveolus, with numerous pigmented cells; on the left, a lymphatic space, with one such cell.

Leucocytes which absorb bacteria certainly, in some cases, become hypertrophied. It is not impossible that, as the bacteria are absorbed and assimilated by the cell, their proteid substances may serve as food for it.

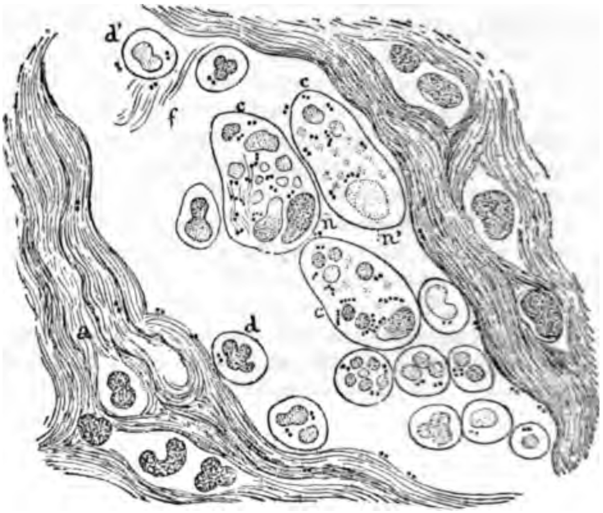
The effect of the bacteria on *tissue-cells* is probably also twofold. It is certain that many are destroyed; this is obvious in all local bacterial diseases. But it is also possible for them to become hypertrophied, as if they had received an extra supply of nourishment.

Whether this is owing to the direct action of the microörganisms, or to the hyperæmia which always results, is difficult to say.

In many of these diseases greatly enlarged elements are seen—e.g. the formation of epithelioid cells and giant cells of tubercle, the inflamed cells of the corium in leprosy and rhinoscleroma (see frontispiece).

Now, in scrofulous inflammations (as was pointed out by Rindfleisch) the cells are of larger size than usual; and, according to Ziegler, this is seen in all chronic inflammations in a greater or less degree. But still a marked increase in the size of elements is very characteristic of chronic bacterial inflammations.

FIG 132.



Suppuration of subcutaneous tissue, caused by micrococci. × 800. (CORNIL and RANVIER).

Section of lymphatic space containing cells. *d*, leucocyte containing cocci: *d′*, leucocyte with pale nucleus, showing necrosis; *c*, *c*, fixed connective-tissue cells, much enlarged, containing several nuclei, of which some (*n′*) are pale and necrotic; also numerous cocci in chains and pairs.

It is disputed whether these large cells are altered leucocytes or tissue-cells. But in the case of the former their large size has one important consequence, that they will be with difficulty removed by the lymphatics, and even if they do get into the vessels will be liable to accumulate in the glands. Hence we see one reason why the cell-products of these specific inflammations are carried away and absorbed less easily than those of common inflammations, and generally give rise to glandular enlargements. It also tends to account for the remarkably permanent character of the tissue-changes, for instance, in leprosy. Other illustrations of the relation of bacteria to cells are given in the frontispiece.

Extension of the Morbid Changes.—The spread of bacterial infection from the point at which it begins is effected partly by the multiplication of the organisms, which takes place with varying degrees of rapidity. But this can hardly be the whole explanation, since we find considerable areas of change, with very few organisms. In acute tuberculosis of man, for instance, many tubercles may be found without bacilli; while other similar ones contain them. In certain cases they are decidedly infrequent, as I can say from my own observations, as well as from the far more numerous examinations made by others—*e. g.*, by Klein, Percy Kidd, etc. It may be supposed that the bacilli in these cases were originally present, but perished. Even supposing this, the influence of bacilli can be traced at distances which, compared with their own size, are considerable. If so, there must be something more than mere contact-action of the bacilli. What is this secondary action?

It may be supposed that the bacilli set up a chemical change analogous to fermentation, which is propagated through the fluids of the tissues. If so, the question arises whether any special substance analogous to a ferment is produced by the organisms, which is the actual virus or poison, and causes the changes set up in the fluids and tissues. This supposition, made by Sir J. Simon and others, has been supported by Dr. Klein.

The physiological ferments—*e. g.*, that of digestion, or Schmidt's fibrin-ferment, which produces coagulation—are formed out of albuminous substances by the action of living cells, such as those of the peptic glands, and the leucocytes of the blood; there is, therefore, nothing strange in the hypothesis that such may be produced by living bacteria. It was pointed out in a previous chapter that abrin and papain, ferments destructive to animal tissues, are formed by vegetable cells.

This supposition, which seems necessary to explain even the diffuse local changes set up by bacteria, becomes still more important when we have to consider the general changes.

General Disturbances Produced by Bacteria.—When microörganisms have set up a local process, there is generally some constitutional disturbance, caused, as we must suppose, by the absorption of poisonous material from the affected spot. Even in diseases which are at first decidedly local, such as anthrax in man (malignant pustule), syphilis, there is some fever to be traced, some interference with the nutrition of the body, though no organism, or very few indeed, can be found in the blood. Death may, under these circumstances (according to Klein), occur within twenty-four hours after inoculation of anthrax into animals. It is clear that the virus is diffused, though the bacilli are not, or only very scantily, so.

The same fact is seen still more strikingly in the specific infective fevers. Death may occur in twenty-four hours in certain cases of smallpox and scarlatina without or before the production of any local symptoms. Hemorrhage is a conspicuous feature in these cases, and points to an alteration in the blood. Rapid death is still more frequent in plague, and the alteration of the blood in this disease is still more noticeable. These are, in fact, cases of death from poisoning, but the poison is the result of the action of the virus of the disease in the blood or tissues. Assuming that these diseases are due to microorganisms, it is clearly not these organisms themselves, but some poison which they produce, which is the cause of death. Such poisons have not, however, as yet been isolated.

The main difference between the specific fevers and local bacterial diseases appears to be that in the former the organisms are diffused by the blood, and set up, beside the local changes, changes in it which may be a part of the disease.

Distribution of Bacteria.—Some of these points have already been discussed in speaking of the special pathology of infective diseases: but a word or two must be said about the manner in which the bacteria themselves are distributed through the body.

Most kinds pass easily into the lymphatics, and thence to the lymph-glands. If they succeed in passing the lymph-glands they may get, by the thoracic duct, into the blood, and thus be carried to every part of the body. In some cases of acute tuberculosis, a special participation of the thoracic duct has been observed. In syphilis the process is equally clear, though the details have not been traced.

Other kinds pass more directly into the veins, and in many cases, if not generally, the machinery by which this is effected is thrombosis. As before described, the microörganisms cause coagulation and penetrate the clot. Then by breaking down of the clot, they are carried into the circulation. This is notably the case with the organisms producing pyæmia. But organisms may enter the veins by ulceration, as has been observed in diphtheritic ulcers of the tonsils.

That microörganisms are in many cases contained in the circulating blood is clear, and they have been, not unfrequently, detected. But it is evident that they must be there in very large numbers, if they are always to be found in the small portion of the blood usually removed for examination. We do not catch fish in every bucketful of water taken out of a river.

When bacteria are circulating in the blood they may become arrested at various points and form secondary deposits of microörganisms, or new foci of disease. This will happen because they form masses too large to pass through the capillaries; and the capillaries of certain parts of the body appear to possess some structural peculiarities, which render them liable to be blocked by such masses, so that capillary embolisms of bacteria are produced.

The block is of course likely to be first found in the first set of capillaries passed through, just as in ordinary embolism. The lungs are thus affected in many bacterial diseases, *e. g.*, glanders, pyæmia, etc., and probably this is the process in some cases of general tuberculosis.

If the bacteria get into the portal circulation, the earliest secondary foci of disease will be the liver. This is seen in abdominal pyæmia, and is possibly the explanation of some obscure diseases of the liver.

If the masses of microörganisms pass through these capillaries, they may be stopped at some point further on. The vessels of the synovia of *joints* appear to have some specific proclivity to form a nidus for the wandering germs of disease. Thus the pyæmic organisms, even when they pass the pulmonary capillaries, may lodge there. The gonorrhœal poison appears to pass into the circulation and settle in the joints. If, as seems probable, acute rheumatism should turn out to be a bacterial disease, it would be a still more striking instance. In suppurative arthritis from scarlatina, and in certain cases an artificial septicæmia, considerable colonies of micrococci have been found in the joints.

The conditions which cause these poisons to be arrested in the joints are probably purely mechanical, since we find that the inorganic poison of gout, urate of soda, obeys the same law. Perhaps it may be that the synovial fringes are liable to pressure, through being *nipped* in the movement of the joint.

Some organisms act directly on the walls of the circulatory apparatus without being blocked, as is the case with the micrococcus producing ulcerative endocarditis.

But in such cases the most important factor in causing the bacteria to settle down at any particular spot, is a damaged or inflamed condition of the part. It is easy to conceive that if the organisms are unable to penetrate the intact vascular walls, they may, when these are damaged, pass through them into the tissues and set up disease. As a matter of fact, we find that a damaged part is likely to be affected by an internal poison just as a wound is by an external poison. Thus ulcerative endocarditis most often affects hearts, the valves of which are already injured by previous disease. A dislocated or strained joint may become tuberculous and so on. A blow on the tibia may, in a syphilitic person, produce a gumma.

Hence it is that common inflammation of a part is so often the precursor and predisposing cause of a specific disease. Thus pneumonia or bronchitis may lead to a pulmonary tuberculosis.

Elimination of Pathogenic Microörganisms.—We might suppose, from analogy, that there would be some mechanism by which the body can get rid of the organisms producing disease, and there is no doubt that some of them do pass out by the ordinary channels, in urine, feces, etc., but this is not quite so general a law as the doctrine of final causes would lead one to expect; just as in the case of mineral poisons nature appears to make an effort to eliminate some but not others.

The micrococci of pyæmia, of diphtheria, and those found in scarlatina, have all been traced in the kidneys, the former distinctly in the urine. The bacilli of anthrax and tubercle have also been seen in the Malpighian tufts, but not in the urine, except when there has been disease of the kidney.

On the other hand, the poison of syphilis does not seem to be able to get out of the vascular system on to the respiratory, intestinal, or urinary surface. As is shown by the remarkable facts of inherited syphilis, the disease may be communicated to the ovum by either parent, but does not affect the fœtus if the mother should become infected while pregnant, as if it could not make its way through the placental vessels.

It is one of the oldest traditions in medicine that diseases which produce an exanthematic eruption are "thrown off" by the skin, which, expressed in modern language, means that the poison or micro-organism is eliminated by exfoliated epidermis or by the cutaneous secretions. Considering the case of syphilis, there is nothing impossible, or even improbable, in this theory; but it is precisely in the case of the skin that exact proof of the elimination of the micro-organism is wanting. Micrococci are said to have been found in the scales in the desquamating stage of scarlatina, but, as before pointed out, the presence of micrococci in the skin is a very ambiguous phenomenon.

The experiments of Wyssokowitsch have shown that bacteria, whether saprophytic or pathogenic, introduced into the healthy body, are not eliminated by any of the secretions, except when a diseased condition of the eliminating organ (for instance, of the kidney) is established, and which leads to some tissue-lesion allowing the micro-organisms to escape. Since, however, it is clear that the parasitic organisms must get out in some way in order to carry on their existence elsewhere, whether in any other host or in a free state, and since the facts of contagion also make some such hypothesis necessary, it would seem that there is here a gap in the life history of pathogenic bacteria left for future research to fill up.

Parasitic bacteria, which live and grow only in the animal body, their state of existence outside being passive or quiescent, may be called endogenic. Those which are capable also of living and increasing in external nature may be called ectogenic. But it is not always possible to say to which class any species belongs.

CHAPTER XLVIII.

SPECIAL KINDS OF BACTERIA RELATED TO DISEASE.

It will now be well to enumerate some of the forms which are definitely related to disease, omitting such as are only interesting from the point of view of natural history, and, indeed, mentioning only those which appear to be of real importance. In Eisenberg's tables of known bacteria, intended for laboratory use, 116 species are enumerated as having been actually cultivated. Of these 70 are regarded as pathogenic, but 27 of these only are connected with human disease; the rest being capable of producing disease in certain animals, but in man of growing as saprophytes only, if at all. The 46 which do not produce any disease are chiefly organisms living free in liquid or solid media; but some few are parasitic saprophytes of man. These numbers are not given as necessarily authoritative; some authors might compile a longer and some a shorter list; but it will suffice to give some notion of the number of forms actually discriminated. The number of actually existing species is doubtless enormously greater.

PATHOGENIC COCCACEÆ.

Cocci of various kinds are frequently found in morbid conditions, and in some cases may be definitely proved to be the cause of the disease with which they are connected; but in other cases considerable difficulties stand in the way of the demonstration. These difficulties arise first from the similarity of form between organisms which have very different properties, so that form alone is an inadequate specific distinction; and, secondly, from the fact that diseased and especially inflamed parts of the body may and do harbor organisms which are not really the cause of the disease with which they are connected.

The confusion arising from similarity of form is to some extent obviated when different species of cocci show different modes of growth, such as into doublets, chains, or heaps—known as diplococcus, streptococcus, or staphylococcus. Such differences may not show any fundamental distinction, but so long as they are constant they furnish convenient marks by which to recognize species.

These do not, however, seem to be necessarily connected with any difference of pathogenic action. The chain forms are met with mostly in fluid, as, for instance, in vesicles or bullæ of the skin, in dilated lymphatic vessels, and so on; while the heaps or masses generally occur in solid tissues, and in thick pus. So in cultivations, chain forms are best produced by growth in fluid media. But very few species are confined to the chain form; and those which are generally found in the form of heaps, often grow at first in the form of chains. Hence the distinction has no absolute validity.

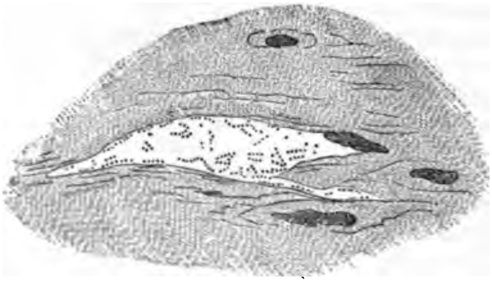
The pathogenic activity of micrococci appears to be always exhibited in the form of acute inflammations of tissue. No chronic inflammatory growths, or granulomata, are known to be produced by them in man: though one such disease in the horse, called mykodesmoid, or discomyces, is attributed to an organism which grows in cultivations in the form of a micrococcus. But as this organism also grows in a peculiar form as Ascococcus, it hardly constitutes an exception. The human pathogenic cocci appear, moreover, to have a short life in the body. It is probable, though not absolutely proved, that they have a non-parasitic life outside the body. But it is certain that they may preserve their vitality in the latter condition possibly as spores.

Among the forms known as streptococcus are the following:

Streptococcus Erysipelatos.—It was first isolated by Fehleisen and Koch from the skin in erysipelas, and has since been constantly found and cultivated by other observers. It forms very small cocci (0.3 to 0.40 μ) which are united in pairs or long chains. It is particularly localized in the lymphatics of skin, and at the boundaries of the erysipelas patch. In fact it is clear that the spread of the micrococcus growth, and thus of the disease, is along the lymphatics and connective-tissue spaces. Cocci are not seen in the lymph-cells, and are rarely, if ever, to be detected in the blood.

In tube-cultivations it forms, after twenty-four hours, white flakes and points along the track of the needle, which afterward run together into an opaque white streak. There is no notable growth on the surface. The growth is slow and succeeds best between 20° and 30° C. It has the power of coagulating milk if grown in that medium.

FIG. 133.



Streptococcus of erysipelas.
Section of lymphatic of the skin containing chains of cocci. × 700. (FLÜGGE.)

The pure cultivation injected into the ear of rabbits produces an inflammation resembling erysipelas, in which the lymphatics are found full of streptococcus, and which is not fatal. In some cases suppuration is produced. Injected into the blood of rabbits it is innocuous.

Inoculations have been made on the human subject, also from cultivations passed through many generations (seventeen or more), and typical erysipelas has resulted after an incubation of fifteen to sixty hours: the beginning of the disease was marked by shivers, rigors, fever, and general disturbance. Persons who had suffered from erysipelas within some months, showed immunity. The inoculations have been often repeated with a therapeutical object, that of curing lupus, cancer, or some malignant new-growth by exciting erysipelas in it; and it is said with good results.

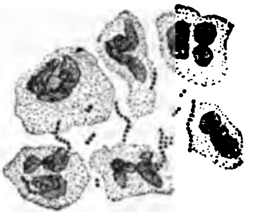
The evidence is therefore very strong that this organism is the real cause of erysipelas, the only doubt being whether it is really distinct from the streptococcus of pus, to be afterward spoken of. There is, however, a difference between the two in their pathogenic action on animals, suppuration being a rare result of the erysipelas cocci; just as it is an infrequent complication of true erysipelas in man; and, when observed, is usually in the lymphatic glands.

The streptococcus has been found by Emmerich and Eiselsberg in the air of surgical wards where cases of erysipelas had occurred (Baumgarten). From this fact and others it would appear that this microörganism is not exclusively parasitic, but may exist as a miasmatic poison, outside the human body, in certain places and at certain times; and the epidemic occurrence of the disease, as well as its prevalence in certain buildings, would thus receive an explanation. It is not, therefore, necessary to suppose that every case of erysipelas is derived from a previous case of the same disease.

Several streptococcus forms are very common in pus, and are readily seen in pustules or inflamed vesicles on the skin.

Streptococcus Pyogenes was first distinguished in pus by Ogston, and cultivated by Rosenbach. It occurs in acute abscesses and in progressive suppuration. The cocci measure 0.6 to 0.7μ or more, and occur singly or in chains up to thirty members. Cultivated in gelatine they do not liquefy it, but form on plate-cultivations round, whitish grains. If sown in a streak the cultivation becomes brownish and swells up in the middle. It also grows on agar-agar and blood-serum, with differences which need not here be described. The most favorable temperature is from 95° to 98° F.; at a lower temperature it does not grow well. The growth is always very slow. In a vacuum this organism converts albumen of white of egg or meat into peptones.

Fig. 134.



Streptococcus pyogenes in pus. × 800. (Flügge.)

The cultivated micrococci inoculated into guinea-pigs or mice produce slowly progressive erysipelatoid suppuration and death. The tissues and abscesses of the inoculated animal show the same cocci.

Streptococcus pyogenes is the organism most commonly seen in cases of pyæmia. It was found by Rosenbach in five out of six cases of mestastatic pyæmia, and in three of these cases no other coccus; in the rest another species (Staphylococcus aureus) was found, though in smaller numbers. In one case the latter species was the only one found. There must be, therefore, some close connection between the streptococcus and pyæmia. But since it is also found in collections of pus which are purely local and comparatively innocent, there must be some mechanical condition which favors the access of the organism to the blood, and the production of the general disease called pyæmia. It has also been cultivated from ulcerated endocarditis, though not the most usual form in that disease. Generally the coccus seems to be connected with diffuse and spreading inflammations more than with well-defined abscesses.

This organism is in form and in the characters of cultivation so much like the streptococcus erysipelatos that many bacteriologists think the two to be really identical. The chief criterion is in the different effects produced by inoculation on animals, and these differences are merely matters of degree.

Another streptococcus obtained by Flügge from the spleen in a case of leuchæmia, and called by him S. pyogenes malignus, also appears to be indistinguishable from the species just mentioned by form or characters of cultivation, but has a much more powerful pathogenic effect on animals. Mice and rabbits inoculated with a small quantity of the cultivated organism died without exception in a few days, having micrococci in internal organs and often in the pus of inflamed joints. It was cultivated from a necrotic mass in the spleen in a case of leuchæmia, a disease which it presumably had nothing to do with causing. A very similar streptococcus (S. septicus) was obtained by Flügge from earth. These species are only important as showing how many closely allied forms, with slightly different pathogenic properties, there are.

Streptococcus Articulorum.—This form was isolated by Löffler from the false membranes of human diphtheria, but there is no reason to think it the cause of the latter disease. A pure cultivation of it, injected into the veins of rabbits, produced purulent inflammation of the joints, and in the pus from these streptococci were found in large numbers. Though the organism is not known to produce suppuration in man, these experimental results have great clinical interest.

Micrococcus Scarlatinæ (Klein).—Several observers have at different times found micrococci in the skin or internal organs of persons affected with scarlatina; but either these results showed obvious elements of fallacy, as in the case of the skin, or else they were believed to be due to infection of the blood with the organisms of suppuration (Streptococcus pyogenes) through ulcers of the tonsils.

Dr. Klein has, however, lately described a micrococcus which he believes to be the cause of the disease. Taking specimens of blood from eleven cases of scarlatina he was able in five to obtain cultivations of a micrococcus which he believes to be specific, while in the other cases no result was obtained. The organism when implanted on the surface of solid cultivation-media grows very slowly in the form of "a grayish translucent film, made up of isolated translucent grayish circular dots," which when numerous are scarcely distinguishable as dots without a magnifying glass. When inoculated by stabbing on the same media it also appears in dots, forming a streak, which when old is slightly brownish. In liquid media, broth or milk, it forms grayish-white fluffy masses. The milk becomes solidified. The form in liquids is that of streptococcus, on solid media that of staphylococcus.

In one of the fatal cases, cocci, chiefly in the form of diplococcus, were found in the cervical lymph-glands and in the bloodvessels of kidney and lung. One of the cases of scarlatina had died from pyæmia.

Cultivations were inoculated under the skin of calves, and mice. There was no suppuration at the seat of inoculation. The calves got thin and had a discharge from the nostrils; some had scurfy patches with loss of hair on the skin, and an eruption on the nostrils. When killed, lesions of internal organs were found, viz.: inflammation of lymph-glands, congestion of liver and spleen, pneumonia, inflammation of the kidneys, and pericarditis. Some of the mice died, and similar visceral lesions were found. These lesions had much resemblance to those of human scarlatina, as least as regards the kidneys.

A similar disease, with the same post-mortem appearances, was produced by feeding calves with cultivations of the micrococcus derived from cases of scarlatina, mixed with milk. Micrococci, corresponding to those of the scarlatinal blood, were found in the diseased organs of the calves, though in small numbers. The micrococci were, however, particularly conspicuous in the affected portions of skin in the calves; and similar appearances were seen by Dr. Kline in specimens of skin from human scarlatina. Cultivations from the blood of dead animals yielded a micrococcus like that of the original cases.

These results had a special interest in consequence of the resemblance or identity of the lesions produced with those produced by a micrococcus derived from a disease of the teats of cows observed on a dairy farm at Hendon in 1885; which disease was believed, by infecting the milk of the cows, to have given rise to cases of human scarlatina. The micrococcus derived from that disease had also the same characters as that derived from cases of scarlatina. Hence Dr. Klein has denominated the organism from these sources micrococcus scarlatinæ.

The intricate questions involved in this case cannot be discussed here; but we must say that the evidence that the milk in the case of the Hendon cow-disease was not infected by cases of human scarlatina is not complete. More recently it has been maintained that the Hendon cow-disease is identical with a comparatively common disease of cows, the existence of which is usually concealed by dairymen for obvious reasons; and this disease Dr. Crookshank believes to be the same as the original cow-pox of Jenner. All that can be said here is that the question is still *sub judice.*

The one point not quite clear in regard to Dr. Klein's micrococcus is whether it is or is not, identical with some other form of streptococcus, especially with Streptococcus pyogenes. Dr. Klein thinks that the details of cultivation and the effects on animals sufficiently distinguish the two forms. Considering, however, the uncertainty felt by many bacteriologists as to the specific distinctness of the various streptococci, and especially since a species believed to be streptococcus pyogenes has several times been found in the bodies of patients with scarlatina, this point seems to require further investigation.[1]

Micrococcus Vaccinæ et Variolæ.—It may be regarded as certain that the virus of smallpox and that of vaccination, are both conveyed by solid particles. In Dr. Burdon Sanderson's words, "the virus is particulate," as was shown by him and by Chauveau, by means of a special method of filtration. Since their researches were made, microörganisms have been demonstrated both in the variolous and the vaccine vesicle. They are cocci, round or slightly oval, single, united in chains or in colonies. No difference can be traced between the cocci of vaccination and those of variola. From the vaccine vesicle it is possible to cultivate several micrococci which grow freely on gelatine. Guttmann found four species, two pathogenic and two not. All attempts to reproduce the lesion of vaccination from the cultivated organisms have at present failed. Proof is, therefore, wanting that these organisms are the cause of the diseases in question; they may be mere innocuous inhabitants of the vesicles, or they may be, as is very probable, sometimes the cause of the suppuration which subsequently occurs.

MICROCOCCI OF SUPPURATION.

It is a matter of no difficulty to detect by appropriate methods the presence of micrococci in almost all collections of pus, large or small, in the human body. The cases in which no microörganisms are found will be considered hereafter.

It is a matter of more difficulty to discriminate the various forms met with; but through the labors of several investigators, especially Ogston, Rosenbach, and Passet, certain forms, apparently true species, have been distinguished which, both in morbid specimens and in cultivations, preserve a constant form and mode of growth.

The following species have been discriminated:

Streptococcus pyogenes.
Staphylococcus pyogenes aureus.
Staphylococcus pyogenes albus.
Staphylococcus pyogenes citreus.
Staphylococcus cereus albus (Passet).
Staphylococcus cereus flavus (Passet).

There are probably other species present in some cases.

The streptococcus has already been spoken of.

Staphylococcus pyogenes aureus is perhaps the most generally distributed of all pyogenic or suppurative bacteria. It was first noticed by Ogston, who gave the generic name; and cultivated by Rosenbach, who called it aureus on account of the golden-yellow color of the cultivations. The separate cocci are spherical, and on the average, .87 μ

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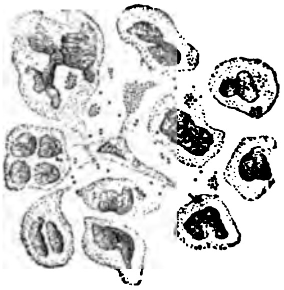
[1] Klein, Supplement to 16th Annual Report of Local Government Board, 1886–7. London, 1887.

in diameter. It grows sometimes in pairs or short chains (Crookshank), but generally forms masses or colonies. It grows somewhat rapidly, and forms on agar-agar by the second day yellow masses. When inserted into gelatine it rapidly liquefies the medium, forming a pit filled with liquid, to the bottom of which the growth sinks after some days as a yellow precipitate. No gas is produced, and there is no odor of putrescence. It peptonizes albuminous substances. The growth has great power of resistance, and may retain its vitality for some months. The best temperature is from 86° to 100° F., but it grows slowly at ordinary temperatures. It can grow with little or no air, but the presence of oxygen is necessary to develop the yellow color.

Fig 135.



Pus with staphylococcus. × 800. (Flügge.)

Habitat.—This organism is found in nearly all collections of pus; most constantly in boils, whitlows, carbuncles, pustules of the skin (impetigo), and in definite circumscribed abscesses of the subcutaneous tissue. In all these it is the predominant organism, but it occurs almost as constantly, along with other cocci, in suppurating glands, empyema, purulent inflammations of joints, and numerous other suppurative inflammations. It is constantly present in acute osteomyelitis, and was at first described as specially belonging to that disease; and is found with other forms in pyæmic abscesses. It occurs only sporadically in the blood of these cases, but is found in most cases of endocarditis. Now it is important to notice that the same organism may be obtained by cultivation from the surface of the body, in moist parts of the skin, especially if dirty, and in matter from under the nails, and has been found in healthy mucus from the pharynx, and in normal saliva. In cultivations of various kinds from the skin it usually comes up along with other organisms. Further, it has been found apart from the human body in "slop" water of kitchens, in the earth, and even lately, it is said, in the air. There is, therefore, great probability that it is widely scattered about in human dwellings, and must be regarded as having an ectogenic as well as a parasitic life.

Pathogenic Effect.—There can be no doubt that this organism is a direct producer of suppuration and is able alone to set up this process. For proof it is hardly necessary to go beyond the experiments which several pathologists have made upon themselves.

Thus Garrè inoculated a small quantity of staphylococcus cultivation into the root of the nail of one of his fingers, and produced a subcutaneous suppuration, in fact onychia. From this he cultivated the S. aureus, and finding that small masses did not succeed, he rubbed a considerable mass of the third cultivation with some force into the skin of his arm. After four days a formidable carbuncle was produced, with some scattered boils, and it was not till after many weeks that the eruption was healed, leaving behind it seventeen scars. A pure cultivation of S. aureus was obtained from the pus. Bockhart applied small quantities of the cultivated organism in a sterilized solution of salt to the skin of his arm, which was in one part slightly scratched, and found small furuncles, but chiefly pustules of impetigo develop even where the skin was quite intact. Examination of the skin showed that the cocci entered the ducts of the sebaceous and sweat glands and sheaths of hair; and where the skin was broken invaded the Malpighian layer of epidermis. The explanation of Garré's results was doubtless that the cocci were firmly pressed into the glands.

Bumm succeeded in producing typical acute abscesses in the subcutaneous tissue of himself and others by injecting with a syringe (under the skin) small quantities of the cultivated staphylococcus along with salt solution. The abscesses were in some cases as large as a fist, and contained the organism in abundance.

Compared with the above results, those of experiments on animals are less important and also less uniform. Mere subcutaneous inoculation produces little effect, but more forcible injection produces suppuration in rabbits and guinea-pigs. The organism injected into the peritoneum produces fatal peritonitis; and introduced into the blood has caused suppurative attacks and inflammation of the kidneys. Endocarditis has resulted if the valves of the heart were injured at the same time. The coccus of osteomyelitis, which is doubtless identical, has produced, when injected into the blood, inflammation of bones, if the bones had been previously injured.

These results are less constant than in the human experiments, and the reason evidently is that the staphylococcus has more affinity for the human tissues, being, so far as it is a parasite, a parasite of man.

It may be asked, if the organism is so frequently present on the surface of the body, why does it not oftener produce suppuration? The reasons seem to be: first, that some kind of wound or else considerable pressure is necessary to enable the cocci to penetrate the skin; secondly, that some skins, for instance those of children, are more easily penetrated, and thus children are particularly liable to impetigo and to "festering" wounds; and, thirdly, there must be conditions, not clearly definable, which make the tissues of some persons, and of the same person at different times, especially liable to the attacks of bacteria or deficient in power of resistance. The facts of contagious suppuration previously stated (p. 356) are explicable as due to the action of this micrococcus, and hardly in any other way; and the same is true of a portion of the process of pyæmia (p. 359); since we must suppose that this, like other parasites, will produce very different results when introduced into the blood or tissues than to those it produces in the skin or external parts.

There can be little doubt of this coccus or allied species being the cause of the suppuration which often supervenes in certain cutaneous affection not at first suppurative, such as acne, herpes, tinea, and in some cases eczema.

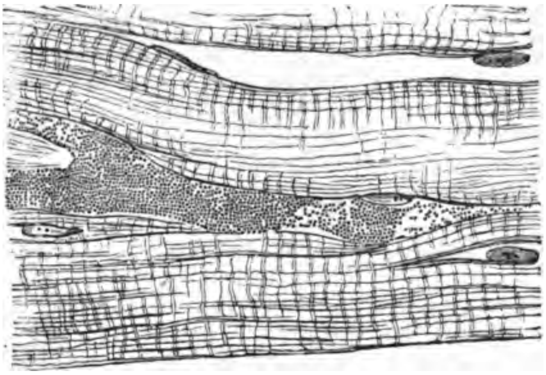
The actual process by which staphylococcus sets up suppuration seems to be chiefly by its solvent and necrotic action on the tissue-elements; and by the injury thus caused to the walls of the blood-vessels, which then permit increased transudation and emigration of leucocytes. It may be plausibly supposed that some enzyme or ferment generated by the bacteria is the actual solvent; but no such substance has yet been isolated.

Two other species, Staphylococcus pyogenes citreus and S. albus, precisely agree with that just described in form and cultivation characters; differing only in color. Their pathogenic effect is also the same; some think less powerful, others more so.

Staphylococcus cereus albus and S. flavus, two species discovered in pus by Passet, much resemble the other forms, but in cultivations do not liquefy gelatine. They have no pathogenic effect on animals.

Micrococci of Endocarditis.—In the ulcerative form of this disease, micrococci are often found on the ulcerated valves, or in the adjacent parts of the heart walls; and there is no difficulty in believing that they are the cause of the disease, which in many features resembles the specific infective diseases, and approaches very near to pyæmia.

FIG. 136.



Micrococci in carditis. × 700 (FLÜGGE, after KOCH).

The cocci have been cultivated, and generally belong to the form staphylococcus, more rarely streptococcus. No specific organism has been found. It is said that the same micrococci occur in some cases of ordinary vegetative (verrucose) endocarditis; but it must be less constantly.

Connection with Suppuration.—That the various pyogenic organisms now spoken of are actually the cause of suppuration cannot be doubted; but it is certain that the process may be set up by other agents. For instance, powerful chemical irritants, such as turpentine, croton oil, carbolic acid, ammonia, when injected into the subcutaneous tissue of animals, with strict precautions to prevent the entrance of bacteria, have produced abscesses ; and it is to be observed that some of the above substances are powerful bactericides, and would prevent the growth of any organisms. Recently the same power has been found to be possessed by a very different substance, cadaverine, one of the ptomaïnes obtained by Brieger from putrid matters, but not poisonous (page 312). This, injected into a sterilized solution under the skin of animals, produced, according to Grawitz, either sloughing or purulent inflammation, or merely inflammatory œdema, according to the degree of concentration. If abscesses were produced, they contained no organisms ; for cadaverine, far from favoring the growth of staphylococcus, is found to stop its growth and kill it.

It would appear, also, that animal parasites, such as cysticercus and echinococcus, have the power of exciting suppuration without the presence of micrococci. But though these other agents are quite possible causes of the formation of pus, micrococci appear to be far the most frequent cause, since Ogston never failed to find some in seventy-four abscesses not previously opened.

Connection with Pyæmia.—This disease has already been referred to as due to external poison or poisons, and doubtless in some of the micrococci we have the poisonous agent. The streptococcus pyogenes seems to be the most important species, but others are found also. Some difficulty will, however, be felt in understanding how these organisms produce a disease so much graver than their ordinary pathogenic effects. One explanation makes the difference a question of dose. A few micrococci entering the blood are lost, but a quantity too large to be at once destroyed establishes itself in the body. There is no evidence that these micrococci multiply in the blood, but they become attached to the endothelium of capillaries, where, if few in number, they may be absorbed and destroyed by the endothelial cells (according to Wyssokowitsch), but if more numerous they block the vessels and lead to the formation of metastatic abscesses already spoken of, so far as these are not produced by direct embolism.

Again, a predisposition to pyæmia is thought to be given by a condition of depressed vitality in the patient as diminishing the power of reaction which the tissues possess. This lowered vitality may result from bad nutrition or from the shock of severe wounds, as is seen in military surgery.

A third concurring factor in pyæmia is doubtless a septic or putrid condition of the wound, its discharges, or some part of the body. It was thought at one time that the bacteria producing pyæmia were the same as the septic bacteria formerly spoken of. But it is clear that the septic species are not the cause of the secondary lesions, at least directly ; and are not present in them. Remembering, however, the action of cadaverine in setting up suppuration, it is probable that ptomaïnes of this class produced in unhealthy wounds and absorbed may have much to do with the formation of multiple abscesses, as well as of fever and general poisoning. Septic organisms and putrefying materials in the intestine have been thought to act as predisposing causes. But in spreading and multiple suppuration, at all events, the micrococci are one indispensable factor.[1]

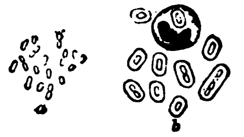
Micrococcus gonorrhœæ (Gonococcus).—This coccus, discovered by Neisser in 1879, is constantly found in the pus of gonorrhœa, and appears to be the cause of the disease. Its diameter is about 1.25 μ. The cocci are usually seen undergoing division, or, it might be said, united in pairs, in the form of Diplococcus. These by lateral extension form flat groups or plates of fours. The cocci grow and multiply within pus cells or sometimes epithelial cells, and are rarely seen free in the secretion. This peculiarity is one which distinguishes them from the cocci of suppuration; from which they also differ in form, and in not retaining the color of aniline dyes when treated with iodine (Gram's method). The organism is very difficult to cultivate, not growing on gelatine, but growing slowly on blood serum. Bumm inoculated a cultivation on the normal urethra with the result of producing acute urethritis.

The gonococcus is only found in gonorrhœal affections of the urethra, the bladder, or female organs; and in specific gonorrhœal conjunctivitis. It is said that the organism has been found in gonorrhœal affections of joints, but in other cases this has not been confirmed. It remains uncertain, therefore, whether these metastatic affections are produced by the same coccus; though the evidence for its pathogenic character in the primary affection is very strong.

Micrococci of Pneumonia.—Several kinds of bacteria have been obtained, either from the sputa or the tissues in acute lobar pneumonia, though it is not clear that the cause of the disease has yet been found.

The species first isolated and recognized was Friedländer's micrococcus or Pneumonococcus, by some regarded as a bacillus. It consists of oval cells, which might be regarded either as oval cocci or short rods, sometimes connected in pairs or short chains. When seen in the lung, the cocci are surrounded by a sort of capsule of considerable thickness. This structure is not peculiar to this organism, since several species of bacteria from different sources show capsules, but serves to distinguish it from others in this situation.

FIG. 137.



Friedländer's pneumonococcus (FLÜGGE). × 700. *a*. From cultivation. *b*. From pneumonic exudation with capsules.

It was found by Friedländer and others in the pneumonic exudation both in sections and in fluid obtained by scraping the cut surface of the lungs. It has also been detected in the sputum of pneumonia, as well as in pleurisy and pericarditis.

It is cultivated easily on various nutrient media, but in cultivations the cocci show no capsules (Fig. 137, *a*). The gelatine cultivation produced by insertion assumes the shape of a round-headed nail. The cultivated organism has been directly injected into the lungs of mice through the chest wall; and all of thirty-two thus treated died in inflammation of the lungs and pleura. The same coccus was found in the lung, spleen and blood, and with a capsule as in the human lung. Rabbits were unaffected. Inhalations of cultivations mixed up with water also produced inflammation of the lungs in mice. While these results show that the organism in question is capable of exciting inflammation and of growing in the tissues of living animals, they do not show it to be the cause of pneumonia, since it is not constantly present; and there are several other species found under the same circumstances.

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[1] On the relation of micrococci to suppuration, see Mr. Watson Cheyne's Lectures on Suppuration and Septic Diseases, Brit. Med. Journal, February 25, 1888, *et seq.*

Diplococcus pneumoniæ.—A coccus growing in pairs, sometimes in chains, up to twenty or thirty members, was isolated by Fränkel, and was independently discovered by Weichselbaum. It forms capsules like Friedländer's coccus; but is distinguished by characters in cultivation which cannot be described here. The cultivated organism injected under the skin of rabbits and mice produces little local reaction, but gives rise to a general septicæmic disease, generally fatal. Pneumonia and pleurisy were set up by subcutaneous injection of a weakened cultivation or by introducing the cultivation direct into the lung.

This organism is stated to be constantly found in the pneumonic lung, and to have a very certain pathogenic effect on animals. It is therefore claimed that it is the specific cause of pneumonia.

Weichselbaum, however, holds that the disease may be produced by several different organisms, of which this coccus is one, and Friedländer's coccus another.

Considering the large part played by cold in exciting pneumonia in the human subject, it does not seem a necessary supposition that there is any one specific cause for the disease. Possibly the cocci which have been found are merely saprophytic inhabitants of the air-passages, which acquire a special vitality in the inflamed lung.

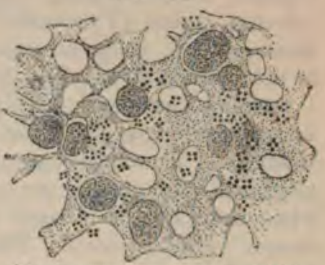
Micrococci of other Diseases.—It should be mentioned that micrococci have been found in several other diseases, and in some appear to be pathogenic; but if so they are not specific, being probably the same forms as have been described in connection with suppuration.

Examples of such diseases are: measles, diphtheria, cerebro-spinal meningitis, trachoma or Egyptian ophthalmia, yellow fever, and others; with regard to all of which the casual relation, as well as the specific distinctness of the cocci met with, are quite uncertain.

A few micrococci which are pathogenic in animals may be mentioned.

Micrococcus tetragenus (*i. e.*, forming tetrads or groups of four).—A small coccus about 0.1 μ in diameter, always arranged in flat plates of four, inclosed in a hyaline capsule. It was found by Gaffky in the wall of a tuberculous vomica in the lung. It has been cultivated and injected into white mice, who die in from three to ten days, showing the characteristic tetrads in all their organs. The common gray mouse is immune. Its importance in human pathology is uncertain, but may often be recognized in sputa of cases unconnected with tubercle, and forms a conspicuous object. Fig. 138 shows the coccus in the spleen of a mouse artificially inoculated. A specimen of lung is shown in the frontispiece. The coccus is stated to be always contained in the bloodvessels.

Fig. 138.



Micrococcus tetragenus. ×600.
(Flugge.)

Micrococcus of Foot and Mouth Disease. From vesicles on the feet of sheep suffering from this disease Klein isolated an organism growing in the form of a streptococcus. Cultures made from this were inoculated into sheep and other animals without effect; but when sheep were fed with the cultures, half of them became affected with a disease of the feet identical with the original. From the vesicles of the experimented animals a streptococcus was cultivated identical in form with the original; and sections of their skin showed the same characteristic changes.[1]

Since this disease has been known to occur in man, these results are not without importance for human pathology.

Micrococcus Choleræ Gallinarum.—This organism produces a disease of poultry called Choléra des Poules, or Fowl Cholera (though it has little resemblance to cholera). It is a coccus 0.2 or 0.3 μ in diameter, usually united in pairs, as a diplococcus. By others it is described as a bacillus 1 to 1.2 μ in length: and indeed if seen with high powers it does look like a rod. It has no interest in human pathology except for the remarkable researches made on it by Pasteur, which are worth study as an example of method (*see* Cornil et Babes, *Les Bactéries*).

Pasteur also discovered a means of attenuating the virus so as to produce something the inoculation of which acts toward the disease as vaccination acts with regard to smallpox; giving immunity against the severer disease.

Micrococci of Septic Diseases in Rabbits.—Koch, by a remarkable series of researches, succeeded in isolating three species of micrococci found in rabbits which were infected with putrid infusions of meat, etc., or with decomposing blood. The one produced death by septicæmia; another pyæmia, and the third progressive phlegmonous suppuration. The same diseases resulted in other animals into which the exudations or blood were inoculated.[2]

Micrococcus Pyocyaneus, coccus of blue pus (Bacillus pyocyaneus, Bacterium æruginosum).—The pus and dressing of wounds sometimes exhibit a remarkable blue color, which is found to depend upon a microörganism thus named, which is by some regarded as a bacillus. It forms short rods or oval cocci. Grown in a tube on gelatine it liquefies this, producing a fluorescent blue color on the surface. The coloring matter (Pyocyanin) can be extracted by chloroform (from bandages, etc., also) and crystallized. The organism is quite innocuous to the wounds in which it grows as a saprophyte (*see* Fig. 122).

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[1] Supplement to Fifteenth Annual Report of Local Government Board, 1885-86. London, 1886.

[2] For details of these important researches see Koch on Infective Traumatic Diseases (Eng. translation), published by New Sydenham Society.

Sarcina Ventriculi.—This parasite, discovered by Goodsir, has been known for many years, but only lately has been ranged among the Bacteria. The characters of the genus have already been given. S. ventriculi is found very generally in the stomach, but is most numerous when the organ is dilated or contains much watery acid fluid in the disease called Pyrosis. There is no proof at all that the sarcina is a cause of disease. It is, however, noteworthy that when cultivated in hay infusion it produces an acid reaction. It has sometimes been found in the lungs, and once in the brain. It can be cultivated on potatoes, and on gelatine plates. The cells are on an average 2.5 μ in diameter, and of a yellowish or brownish color, arranged in square packets of eight. A much smaller species, Sarcina urinæ, has been found in the urine. Several others are known, from water or air.

PATHOGENIC BACILLI.

Before studying these organisms, which produce some of the most important of parasitic diseases, it will be well to be acquainted with a common non-pathogenic form which is a good example of the genus.

Bacillus Subtilis, or the hay-bacillus, is an almost universally diffused species, which may be obtained for examination by infusing a little hay in water. If the infusion be boiled, other organisms will be killed, but Bacillus subtilis survives. On filtering the solution a nearly pure cultivation is obtained. It is also found with other animal and vegetable forms in any water containing dead vegetable matter, such as flowers. The rods measure up to 6 μ long, and about 1 or 2 μ broad. They are mobile with flagella, and grow into long segmented threads, the segments having rounded ends. They also form spores. These processes may be well studied in a drop of hay infusion, especially if the bacilli be colored with a little methylene-blue, fuchsine, or other dye. It is to be noted that the spores are not colored by the ordinary process, but may be so by heating in a solution of fuchsine for twenty minutes. A drop may be dried on a cover glass and mounted. The study of this common object is a good preparation for the study of pathogenic bacilli. It may be cultivated on potatoes, gelatine, etc.

The following species of bacilli will here be noticed :

Pathogenic in man.

Bacillus anthracis.
" tuberculosis.
" lepræ.
" mallei (of Glanders).

Bacillus typhosus (of Typhoid Fever).
" œdematis maligni.
" diphtheriæ.
" syphiliticus.
" rhinoscleromatis.
" malariæ (?).

Occurring in morbid conditions, probably saprophytic.
Bacillus Neapolitanus (Emmerich).
" of human septicæmia (Klein).
" pyogenes fœtidus.

Pathogenic in animals.
Bacillus of swine plague.
" of tetanus.
" of ulcerative stomatitis in the calf.
" of septicæmia in mice.
Bacillus (clostridium) of symptomatic anthrax.

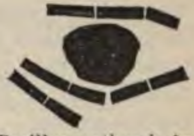
Putrefactive or Zymogenic.
Proteus mirabilis et vulgaris.

BACILLUS ANTHRACIS.

This organism is found in the blood of animals and men affected with the malady called Anthrax or Splenic Fever. The human disease is known as malignant pustule or Woolsorter's Disease, and in Russia as Siberian plague (see p. 386).

The bacillus was briefly mentioned by Rayer and Davaine in 1850; afterward more fully described by Pollender in 1855; and again by Davaine in 1864. Since then it has been studied by many observers, especially by Koch and Pasteur.

FIG. 139.



Bacillus anthracis in blood. × 1200. (CROOKSHANK).

The bacillus is, from its comparatively large size, more easily seen than most. The rods are 3 to 20 μ long and 1.0 to 1.2 μ thick, with sharply truncated ends. They divide when they have doubled their length, but when cultivated at 96° F. in nutrient fluids grow out into long, often convoluted, threads, in which the individual elements are still sharply distinguished. After a time the formation of spores commences. Spore-formation is possible at any temperature between 60° and 110°, but only provided there be free excess of air. Hence spores are formed in cultivations on solid media, or on the surface of fluids, but not any depth below the surface.

The spores are formed from the internal protoplasm of the rods; they are oval, about 2 to 3 μ long and 1 μ thick. They are not stained by aniline dyes with the ordinary processes, and hence look like colorless dots in the rods; but when exposed to a hot solution of fuchsine for twenty minutes or more they may be stained red, as seen in the frontispiece (Fig. 5). The spores were shown by Koch to grow again into rods.

The bacillus requires air, or at least scarcely grows if entirely deprived of it, but a small supply will suffice. The minimum temperature for its growth is about 54° F.; the maximum 108°. Growth is arrested by freezing, but the vitality not destroyed. Drying up kills the bacilli, but not the spores. In dead animals the bacilli die if secluded from oxygen, and undergo degeneration till they entirely disappear from the organs and blood after five to eight days (Klein). But Koch found that large masses of affected organs might preserve some virulence for four or five weeks. The bacillus is killed by a temperature under boiling point. Spores exposed to moist heat at 212° are killed after fifteen minutes, but in the dry state they survive exposure to the same temperature for an hour.

Cultivation Experiments.—The bacillus forms, in plate-cultivation, round dark greenish-black colonies, which are just visible after twenty-four to thirty-six hours, and as they enlarge become surrounded with a wavy outline, which under the microscope is seen to be composed of threads, like locks of hair, passing out in all directions, so as to form a flocculent mass of a grayish color. It slowly liquefies the gelatine.

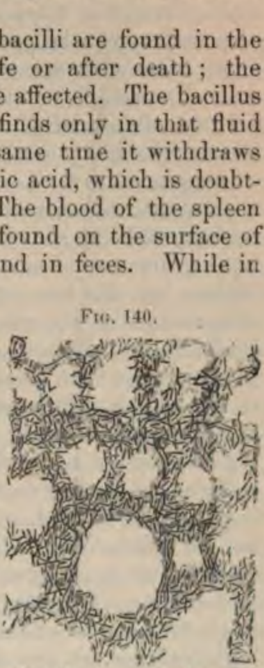
If inserted into tubes containing nutrient gelatine, "a whitish line develops in the track of the inoculating needle, and from it fine filaments spread out in the gelatine. Occasionally an isolated spot develops, from which rays extend in all directions like the filaments of thistle down. In more solid nutrient gelatine the growth appears only as a thick white thread" (Crookshank). As the gelatine liquefies, the growth subsides as a white flocculent mass. On nutrient agar-agar a white film is developed. The bacillus grows very well on potatoes, and forms a creamy layer which spreads over the surface. Spores are produced with free access of air, and may be preserved on silk threads which have been soaked in the bacterial film. On coagulated blood serum it grows, producing liquefaction. The production of spores takes about twenty hours at 95°; but is slower at lower temperatures. Deprivation of light retards their development. The process may be followed in a "hanging drop" of nutrient fluid under the microscope.

Inoculation Experiments.—The smallest quantity of blood from an animal suffering from anthrax, if injected into a rodent reproduces the disease, usually causing death in about forty-eight hours. The blood of the inoculated animal, inflammatory exudations, and urine contain the bacilli. Precisely the same results follow the inoculation of bacilli, or their spores from a cultivation. Dogs, cats, and pigs are insusceptible; rats are not easily infected.

The local lesion produced at the point of inoculation is very slight. Infection may take place through the respiratory or intestinal tract, but less easily than by inoculation, spores being specially efficacious. Inhalation of spores has produced the disease; and Koch caused anthrax in sheep by making them swallow potatoes containing spores. Bacilli without spores did not have the same effect. The spores once arrived in the intestine rapidly germinate and spread in the bacillar form into the bloodvessels.

Distribution of Bacilli in the Body.—The bacilli are found in the blood, where they may be detected during life or after death; the cells and tissues are in the general disease little affected. The bacillus is thus chiefly a blood-parasite, and probably finds only in that fluid the amount of oxygen it requires. At the same time it withdraws oxygen from the blood and substitutes carbonic acid, which is doubtless partly the cause of its injurious effects. The blood of the spleen contains the largest numbers. They are also found on the surface of the lung-alveoli and air-passages; in urine and in feces. While in the body, the bacillus never forms spores, but does so rapidly when it escapes into the air by any of the excreta.

FIG. 140.



Distribution of anthrax bacilli.

Section of lung of rabbit affected with anthrax, showing bacilli filling the pulmonary capillaries.

When the bacilli are first received into the body by inoculation, as in the "malignant pustule" of man, they cannot produce an entirely local effect, and cannot at first be detected in the blood. When once bacilli have appeared in the circulation, the disease is incurable; but they often appear there, in the human as well as in the inoculated disease, only a short time before death.

Anthrax in the Human Subject.—The disease in man occurs as "malignant pustule" and as "internal anthrax."

The former is a local inoculation of spores of the bacillus from fleeces or hides of animals dead of anthrax. It forms a pustule, followed by local gangrene and other symptoms which need not be described here. The diagnosis is certain by the discovery of bacilli. This affection is not seen in the lower animals.

In internal anthrax the poison affects chiefly the respiratory or the gastro-intestinal system respectively. The respiratory form of the affection has been known as Woolsorter's Disease, being acquired through the inhalation of dust containing anthrax-spores by those engaged in unpacking bales of foreign wools at Bradford. It was investigated by Dr. Greenfield and Mr. Spear. Another form affects the larynx, pharynx, and adjacent parts of the neck; a case of which came under the observation of the writer in Southern Russia in 1879. Inflammation of the affected organs occurs, with a great amount of inflammatory œdema of all surrounding tissues, which is a very characteristic feature. The intestinal form is very rare in man, but has been observed.

General Biology of the Bacillus.—It is an important question how the bacillus lives in the period intervening between its leaving one animal body and entering another, since it is not very frequently transferred by direct contagion. For its preservation, spores are necessary; the simple rod-form, as in blood, soon dies if dried up, but when spores are once formed, they may be subjected to great dryness and extremes of temperature without losing their vitality. How long this vitality can be preserved it is impossible to say, but certainly at least from one year to the next. Spores are formed whenever any animal secretion, or blood containing them, comes in contact with the air immediately after the death of the animal. They are not formed within the body of the animal, and if this be buried intact, spore-formation is, so far as that is concerned, prevented; but it is obvious that accidental circumstances might bring the contained bacilli in contact with the air. Pasteur has supposed that spores may be formed in the carcasses of buried animals and brought to the surface by earthworms, but this has not been confirmed. In northern climates, if the temperature of the subsoil be under 45°, no growth takes place, and probably the bacillus soon dies; but if spores have been formed, and the carcasses have been opened, it will remain as a focus of infection in the soil, even for some years.

Spores may remain, probably, for a long time without germinating; but in summer, when the temperature is high enough, and if there is sufficient moisture present, germination may take place in the soil, rods may be formed, which again form spores, and thus the organism will be multiplied. The whole life-cycle may be gone through in from twenty-four to forty-eight hours (Koch). However, it is clear that germination and growth will take place even more rapidly and certainly if the spores be received into the body of a sheep or ox, with its high temperature and abundant supply of nutriment.

The bacillus anthracis is thus not a complete or obligatory parasite, since it has also an ectogenous existence; but is an occasional parasite. At the same time it is probable that a parasite's life is favorable to its multiplication and to its distribution.

Vaccination of Anthrax.—Just as in smallpox we have in virus obtained from the cow a means of setting up a mild disease which gives immunity, so Pasteur has elaborated a method for obtaining an attenuated virus of anthrax, which, inoculated into cattle, gives them immunity against the ordinary malignant virus.

The same method has been applied to other diseases, viz., to fowl-cholera, swine-plague (Rouget du Porc), symptomatic anthrax or quarter-evil; and lately the same result is said to have been obtained for hydrophobia.

Pasteur's general method of attenuation or production of a vaccine consists in cultivating the organism in such a way as not to produce spores. This is effected by keeping a cultivation of anthrax bacilli in chicken broth at a temperature of 107° to 109° F. in contact with air. Under these circumstances they die after a month or six weeks, but in the meantime the virus is "attenuated," or less malignant. Cattle or sheep inoculated with material thus treated for twenty days, acquire a slight illness which gives them immunity against the true anthrax. To render the immunity more complete, they are inoculated a second time with a virus less attenuated, and after this they are insusceptible of true anthrax for the space of about a year, a period long enough for breeding and fattening some domestic animals.

Toussaint had previously obtained an attenuated virus by heating infected blood containing bacilli for ten minutes to 130° F. Chamberland and Roux got similar results by adding antiseptics, such as carbolic acid, in small quantity to the virus. Chauveau heats blood containing anthrax for twenty hours at 107° to 109°, and then after an interval for one, two, or three hours, the degree of attenuation being proportioned to the time during which it is heated. The bacilli multiply and produce generations showing the same modified virulence, and the spores formed by them, if heated one hour at a temperature of 170°, are found to be free from virulence in the same degree.

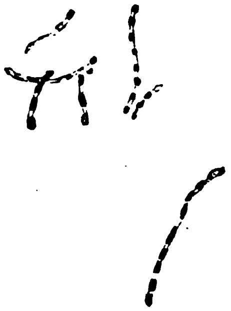
Inoculations with the "vaccine" or modified virus have been carried out on an enormous scale, hundreds of thousands of sheep and cattle having been thus treated; and though exception has been taken to some of the scientific data on which the practice is founded, it appears to be of great economic value. The chief practical objection made by Koch is that the vaccine, to be of any use, must be strong enough to produce death in some cases; and the mortality from this cause may be greater than that which it is intended to prevent. The same result is attained by passing the virus through certain species of animals. The virus obtained from white mice affected with anthrax is not fatal to sheep and cattle, but gives them immunity (Klein), and the blood of guinea-pigs with the same disease does not, as a rule, kill cattle. These results only apply to ruminants. Rodents have no immunity, for though the anthrax virus may be attenuated by heating till it is not fatal to these animals, they are, after inoculation with it, as liable to true anthrax as before (Klein).

BACILLUS OF TUBERCLE.

Several observers had observed bacteria in tubercles before Koch, in 1852, published an account of this organism, which is now universally recognized as the cause of tubercular disease. Baumgarten appears to have seen the same bacillus, but had not given any proof of its pathogenic character. Koch not only detected the bacillus, but at the same time showed how it could be recognized by color reactions, cultivated, and proved experimentally to be the cause of the disease in question.

Bacillus tuberculosis is one of the smallest bacilli; it is a motionless rod measuring two to five μ in length (that is, one-third or one-half the diameter of a red blood-corpuscle), and about one-sixth of its length in thickness, with rounded ends. It sometimes, but not always, shows, when stained with aniline dyes, a beaded structure with alternation of colored and uncolored portions. The ends are always colored; the number of intermediate colorless portions being from three to six, or rarely more. This condition has been regarded as indicating spore-formation, but there is not an agreement as to whether the stained or unstained elements are the spores. Koch suggests the latter, from the analogy of the anthrax-bacillus, but the high power photographs of Dr. Crookshank seem clearly to show that the bacillus consists of a series of granules enclosed in a sheath, with intervening parts which do not take coloring matters. The stained elements would then be the spores, if spores there are; or possibly, as Dr. Crookshank suggests, only certain of them, somewhat larger than the rest, are so.

Fig. 141.



Bacillus tuberculosis, from sputum. × 2500. (Crookshank, from photographs.)

The resemblance of such bacilli to a chain has suggested such a hypothesis that they really are chains of micrococci, like a streptococcus. But minute examination with the best powers negatives this supposition.

The beaded or spore-containing bacilli are constantly seen in sputa, and also in caseous tubercular products; Baumgarten affirms that they are also found in old cultivations of the bacillus, but that recent cultivations, as also recently inoculated tubercle (of animals), furnish continuous rods only. The question is, however, not yet at rest. The tubercle-bacillus has no other peculiarity of form, except that the rods in sputa are often slightly curved; but it is recognized by its relations to the aniline colors, which will be spoken of afterward.

Cultivation of the Tubercle-bacillus.—Its cultivation is rather difficult, as it will not grow in nutrient gelatine, and scarcely on agar-agar, nor at ordinary temperatures on any medium. Tubercular matter implanted on sterilized, solidified blood serum in a tube or shallow cell, and kept at a temperature of 98.5° to 102°, begins to grow slowly, and after ten to fifteen days small, whitish scales are seen. These increase till a thin, whitish layer spreads over the surface of the medium. If accessible to microscopical examination with a low power, this is seen to consist of masses of bacilli arranged in spiral or curved lines, their long axes in the same direction. This arrangement is well shown in an "impression," that is, a portion of the layer removed on a cover-glass, and is remarkably like a growth of the hay-bacillus in water. After about a month they cease to grow, and new cultivations can be set up by planting a minute portion in another tube. In this way successive generations may be produced, and the organism kept alive for months or years, without change in its form or mode of growth.

The optimum temperature is about 99.5° F., and of course a little variation from this on either side retards the growth. There is no growth below 82° nor above 108°. The medium has to be kept from drying up, and the addition of a little glycerine is said to favor the growth. Cultivation is effected with difficulty in liquid, such as broth, a white granular precipitate being formed after four or five weeks.

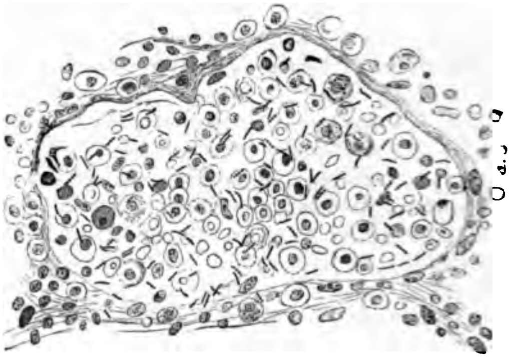
These cultivation experiments are very important in relation to the natural history of the bacillus, showing that its conditions of growth are confined within very narrow limits, and that a saprophytic vegetation in external nature is, in our climate at least, impossible. The bacillus is, therefore, a true or necessary parasite of men and other animals. At the same time the bacilli are found to have great power of preserving their vitality when dried up, or when exposed to considerable vicissitudes of temperature; so that those which are ejected with sputa, whether they contain spores or not, presumably retain the power of germination if again introduced into the human body. Dried bacilli usually lose their power of infection after about six months in a dry state. A boiling temperature has to be kept up ten minutes in order to kill them. Steam at 212° destroys the vitality of bacilli in sputa in fifteen minutes if moist, but half an hour or an hour is requisite if in the dry state. Putrefaction of sputum kills them after some days. Gastric juice has no traceable injurious effect.

Relation of Bacillus to Tissue.—The manner in which the bacillus gives rise to a tubercle has been closely studied by Baumgarten in tubercles produced by inoculation in the rabbit's eye. There is no doubt that the bacillus acts like a foreign body or irritant (see p. 367), but with certain special properties. The bacilli, when introduced, multiply and spread through the surrounding tissues—not, as Baumgarten believes, by the agency of leucocytes, but along the ordinary lymph spaces and channels. On the sixth day visible tubercles appear, and are found at first to consist entirely of *epithelioid* cells, which are produced in large numbers. Baumgarten attributes their production to proliferation of the fixed tissue cells, in which signs of nuclear growth (karyokinesis) are visible even then, and still more in the next few days. Migratory leucocytes first appear at a later period—on the tenth or eleventh day after inoculation—when the signs of vascular inflammation (hyperæmia, etc.) are visible; but they may then infiltrate the tubercle so as to seem the predominating element, forming the so-called lymphatic tubercle.

The formation of giant cells is, according to Baumgarten, a variable element in tubercle production. They are usually even absent when a fragment of human tubercular tissue is used for inoculation, but numerous when bovine tubercle is the irritant, or when artificial cultures of tubercle are used. The explanation he gives is that only a weak or modified action of the bacilli gives rise to giant cells, which show a sort of temporary arrest of growth; while in a more intense action the cell-production is too rapid to admit of their formation. One peculiarity should be mentioned as to giant cells, which constitutes a difference between human tuberculosis and that of some animals. In specimens from the human subject the giant cells very rarely contain bacilli. The writer has never seen them in that situation, and observers of much larger experience have confirmed this. negative result. On the other hand, in inoculated tubercle, and in the spontaneous disease of some animals—for instance, of cattle, poultry, horses (see frontispiece, Fig. 4)—bacilli are very abundant in giant cells. No satisfactory explanation has yet been given of this difference. The bacilli are, on the other hand, very numerous in t caseous masses of human phthisis.

However this may be, it would seem, if **Baumgarten** is right, th the tubercle-bacillus acts as a direct stimulant of growth and pro eration, and not, like some other organisms and chemical irritan merely in the way of producing injury and necrosis. Degenerati

FIG. 142.



Tubercle-bacilli in alveolus of human lung (PERCY KIDD). From specimen of catarrhal pneumonia.

necrosis, and caseation are nevertheless constant phenomena in tuberc and never long delayed. They begin in the centre of the tuberc and soonest in those which are infiltrated with migratory lymph cel

Recognition of the Tubercle-bacillus.—It may be recognized sputum, for instance, by solution of potash, which dissolves ot elements and leaves the bacilli; but this would not distinguish t tubercle-bacillus from many others. It is, however, distinguish from all, except the bacillus of leprosy, by certain relations to anili dyes. It absorbs these colors—for instance, fuchsine and meth violet—more slowly than some other organisms, but retains them wi greater tenacity. If, then, a cover-glass preparation or section stained deep red with fuchsine, and then treated with a dilute miner acid, the color will be discharged from every part of the preparati except from the tubercle-bacilli, which remain red. Or if the stain preparation be treated with a solution of methylene blue (or of ce tain other dyes), this color will replace the fuchsine in all elemen except the tubercle-bacilli. There are many variations of these pr cesses, some of the more important of which are described in t appendix.

Proof that the Bacillus is the Cause of Tubercle.—We have see in speaking of tubercle that there is strong evidence of its being a infective disease caused by some living virus. The next and cruci question is whether the bacillus now spoken of is or produces viru The reasons for concluding that it is are as follows:

The bacillus is found in all cases of tubercular disease carefully examined. In animals it is found almost universally in all affected tissues, in man in at least some of them.

A scarcely visible portion of material containing bacilli is taken, and cultivated apart from the body. It increases to a conspicuous and ponderable mass, which may be (say) a hundred times larger than the original fragment. A very small portion of this is taken and cultivated again till it increases in the same ratio, and so on for several times. If anything else derived from the original body were adhering to the bacilli this would now be diluted in an inconceivable degree. A small portion of the mass of bacilli resulting from these cultivations is introduced into (suppose) the eye of a rabbit. Tubercle is produced there, and the disease extends through the body of the animal till it kills it. The same bacilli are then found in all the affected tissues of this animal, and may be used to effect further cultivations.

Koch's fundamental experiments were conducted on a very large scale. He obtained cultivations from forty-three original sources, of which twenty-two were taken direct from tubercular material; fourteen of these being from human morbid products, including pulmonary phthisis, miliary tubercle, scrofulous glands, lupus, etc. The remaining twenty-one cultivations were derived from guinea-pigs which had been previously inoculated with tubercle from human or animal spontaneous disease. There was no difference between the bacilli obtained from all these sources, nor was there any change visible in the cultures, however long carried on.

In inoculation experiments the greatest care was taken to avoid three serious sources of error: first, mistaking spontaneous tuberculosis for that artificially conveyed; secondly, confounding tubercular products with inflammatory matters produced by other causes; and thirdly, the unintentional infection with tubercular matter by means of impure instruments or material. Each of these sources of error had been found to interfere with the value of previous researches.

Inoculations were then made both with tubercular products which were proved by microscopical examination to contain bacilli, and also with pure cultivations of the bacillus.

The method of procedure was in the first class of experiments to insert fragments of tissue into a little pouch made by a short incision into the abdominal wall of a guinea-pig. The inoculation wound healed on the next day, and showed no reaction. Generally it was not till after a fortnight that some swelling of the nearest lymphatic glands occurred, and at the same time induration took place in the inoculation wound, which afterward broke down and became converted into an ulcer. The animals began to lose flesh, their coat became bristly, dyspnœa set in and they died or were killed between the fourth and eighth weeks. Other inoculations were made in the anterior chamber of the eye.

In the second class of experiments with artificial pure cultures similar results were obtained, the animals becoming affected with miliary tubercle, and not only those very susceptible of tubercle, such as guinea-pigs, but even dogs, rats, and white mice, which are, as a rule, little subject to tuberculosis, could not resist infection with large quantities of tubercle-bacilli.

Control experiments were made with a large number of pathogenic and non-pathogenic bacteria, which were inoculated in the same way, but in no case produced tubercle.

These experiments of Koch's have now been so often repeated, and confirmed by pathologists in various parts of Europe, that it is unnecessary to give further details.

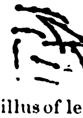
The general result of these experiments is not merely to show that tuberculosis is a specific infective disease, for that might be established without reference to bacilli: but to show that all agents which produce tubercle contain the bacillus; and this, therefore, is the only essential cause of the disease.

Predisposition.—Different species of animals show very different degrees of susceptibility to tubercular infection; that is, they do not present equally favorable soil for the growth of the tubercle-bacillus. Most rodents are very susceptible, and thus inoculation experiments always succeed with them. Ruminants are also for the most part susceptible; so are monkeys; carnivora, at least dogs and cats, much less so.

The human race is evidently susceptible, but since we do not try inoculation experiments on man, we cannot tell whether he is susceptible in the same degree as rodents. What is, however, certain is that there are great differences of individual predisposition. Some persons have an organization fitted for the growth of tubercle-bacilli; others not. If all persons were equally liable, the disease would be nearly universal. But it may be doubted whether these differences are more striking as regards tubercle than as regards many other maladies. A certain proportion only of those persons who are exposed to the infection of any of the specific diseases acquire them, even when they are epidemic. If every person were equally liable to every contagion, it might easily be shown that the whole population of a country must sooner or later be infected with every endemic disease.

Bacillus Lepræ.—The bacillus of leprosy much resembles that of tubercle. It is a slender rod 4 to 6 μ in length, less than 1 μ thick, or about one-half or three-fourths the diameter of a red blood-disk. It shows no movement. Two or three spores are sometimes formed in the interior, which cannot be colored by aniline dyes. In all its reactions with coloring matters it agrees with the tubercle-bacillus, but also takes on such dyes as stain the nuclei of cells. Cultivations have not succeeded, though in blood-tissue a slight liquefaction is said to result after a week, and thus the original fragment may slightly increase in size. Inoculations on animals have given ambiguous results, some local changes being produced but no general disease. In its relations to the tissues this bacillus shows some remarkable features. The first is the extraordinary number in which it occurs. In leprous skin, "almost the larger half of the tissue consists of

FIG. 143.

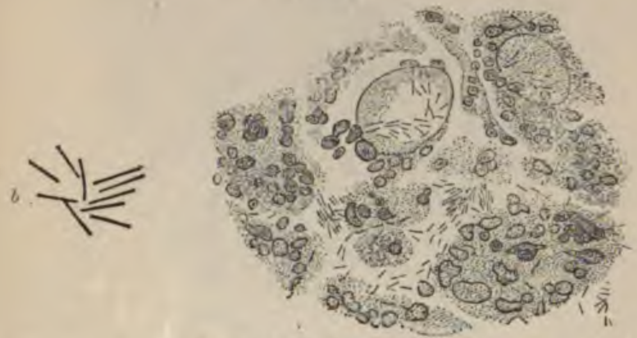


Bacillus of leprosy. × 1200. (CROOKSHANK.)

bacilli and their products" (Unna). In sections the bacilli appear in large masses which are generally regarded as cells, though the occurrence of the bacilli in cells has been denied by Unna. It is difficult, however, to interpret in any other way such appearances as those seen in the frontispiece (Fig. 3). The bacillus is also found in the sheaths of nerves affected with the special morbid change, and in all tissues which are altered in the same way.

Bacillus of Glanders (*B. mallei*).—This is about the size of the tubercle-bacillus, but thicker, and is highly motile. It forms spores. It was found in the characteristic nodules of glanders in horses by Schütz and Löffler, and has since been shown to occur in human glanders. It has been cultivated, and when inoculated into horses, rabbits, guinea-pigs, and mice has produced a disease with ulcers and nodules like those of glanders. The bacillus has been found in the diseased tissues and organs of these animals, as also in their blood and urine, so that the proof is complete that the bacillus is the cause of the disease.

FIG. 144.



Bacilli of glanders (FLUGGE).
a, section of a nodule × 700. *b*, bacilli colored with methylene blue × 1500.

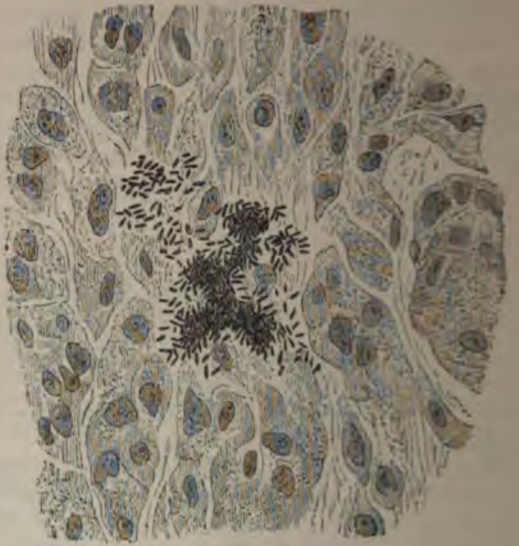
It may be cultivated on gelatine, agar-agar, or blood-serum at about 99° F., but grows slowly. It is said to grow even at ordinary temperatures on agar-agar mixed with glycerine, minimum temperature 77°, maximum 110°.

Bacillus of Typhoid Fever (*B. typhosus*).—Several observers, Weigert, Klebs, and Koch, have found bacilli in the Peyer's patches, mesenteric glands, and spleen from cases of typhoid; but a species observed by Koch, and restudied by Gaffky, appears to be the only one constantly and exclusively present, having been found by Gaffky in 26 cases out of 28 examined—a result confirmed by other observers. Moreover, the same species is not known to occur under any other circumstances.

The bacillus is 2 to 3 μ long, and about one-third of its length in thickness, with rounded ends. It is capable of growing into pseudo-filaments, and sometimes occurs in very short rods. It is highly

motile, and probably possesses flagella. It is stained with diffic
a long action of the usual dyes being necessary.

FIG. 145.



Bacilli of typhoid fever (FLÜGGE).
Section of spleen × 800.

In plate-cultivations on gelatine it forms superficial grayish-wh
colonies with sinous outline; and if inserted into tube-cultivatio
grows chiefly on the surface, producing a similar form. A very cha
acteristic form of growth is that on potatoes, which is thus describe
There is no visible growth after forty-eight hours, but the surfa
looks moist and glistening. On touching it with a platinum nee
the surface gives the impressions of being covered with a hard resist
film, and this on examination is found to be made up of long thre
of the bacilli containing spores. On potato-paste a visible yellow
culture is obtained (Eisenberg). The characters of cultivation
potatoes are regarded as diagnostic.

The growth does not liquefy gelatine. The best temperature is 9
to 104°, within which limits terminal spores are formed in three
four days.

The bacillus has been found in the dejections, in the blood and
albuminous urine of typhoid patients during life, as well as in vario
organs *post-mortem*. It has not been detected with certainty in wat
or elsewhere outside the human body.

Experiments on animals have been uniformly unsuccessful, f
though they have sometimes died, the characteristic lesions of typho
have never been produced. Still, considering the facts above-men-
tioned, and since this bacillus differs from any of the known sap-

phytic species found in the intestine, there is a considerable probability in favor of its being really the cause of the disease.

Bacillus Œdematis Maligni (Bacillus of progressive gangrene; *Vibrion septique*).—An organism first described by Pasteur as producing a form of septicæmia in animals; afterward isolated by Koch from garden mould, and found to produce the affection called malignant œdema in rodents. This disease seems to be identical with a form of traumatic gangrene, characterized by crackling emphysematous distention of the cellular tissue with gas (gangrène gazeuse), which occurs in complicated or neglected wounds. The identity of the human and the artificial rodent disease has been established by inoculation and culture.

The bacillus much resembles B. anthracis, but differs in forming threads while in the blood. Spores are produced singly in each rod, which becomes expanded in the middle or at one end before spore-formation. The rods are easily colored with various dyes. For the characters of cultivation reference must be made to special works. The optimum temperature is that of the human body.

The bacillus is important on account of its very general distribution in external nature. It is found in nearly all putrid substances, in soil which is impregnated with filth, in the dust of hay, and even in the dust of rooms. It is also obtained from the bodies of animals killed by strangulation if kept warm after death. A very small quantity of earth containing it, if inoculated under the skin of a guinea-pig, causes death in a day or two; and the bacillus can be further cultivated from the dead body of the animal.

Bacillus Diphtheriticus.—It has been already mentioned that various organisms are found in the membranes and necrotic tissues of diphtheria, but they are for the most part evidently mere inhabitants of the dead tissues, and not the cause of the disease. Löffler has isolated from the deeper layers of the false membrane, verging on healthy tissue, a bacillus which is certainly pathogenic in animals, though it is not proved to be the origin of the diphtheritic process.

It is a rod, sometimes slightly curved, as long as the tubercle-bacillus, but twice as thick, which shows no spontaneous movement. No formation of spores is known. It may be cultivated at temperatures over 68°, best at 99°. The best medium is blood-serum, made nutrient with "saccharine peptonized infusion of meat."

Inoculated into guinea-pigs it caused death in a few days. When it was introduced into the trachea of fowls, pigeons, and rabbits, false membranes were formed, sometimes very extensively, and the same were produced on the slightly wounded conjunctiva of rabbits. These membranes, however, contained few or no bacilli. Moreover, the bacilli were not found in a series of well-marked cases of human diphtheria. In addition, Löffler, on examining the mucus from the mouth of 30 healthy persons, succeeded in one instance in isolating this very bacillus. On all these grounds the discoverer of the organism hesitates to conclude that it is really the cause of diphtheria.

The etiology of this disease remains an unsolved problem. Possibly the explanation of some of the difficulties met with in its solution: that there are really several distinct affections comprised under the same name, a supposition confirmed by the wide variations observed in the gravity of the cases which are clinically regarded as diphtheria.

Bacillus Syphiliticus.—Many attempts have been made to discover microörganisms in the lesions of syphilis, but only lately with any success.

Lustgarten was the first to describe a bacillus which he detected in every one of sixteen cases by a special method of coloration.

This organism is described as somewhat like the tubercle bacillus, occurring in slightly curved rods of 3 to 7 μ in length, which, with very high powers, show uncolored spots supposed to be spores. They never occur free in the tissue, but only in groups within certain cells forming part of the syphilitic granulation-tissue. The number of such cells found was, however, extremely small. Several other observers have seen apparently the same bacilli and found other ways of staining them. They have never been cultivated. Some doubt has been cast upon the specific character of these organisms, because very similar bacilli have been found by Alvarez and Travel in the normal smegma præputii. Moreover, other observers have entirely failed to find bacilli by Lustgarten's methods.

Recently, Messrs. Eve and Lingard have succeeded in cultivating as well as demonstrating a bacillus from syphilis which does not appear to be identical with that of Lustgarten. They demonstrated bacilli in at least twelve primary sores, in three cases of indurated glands, in two cases of gummata, in a papular syphilide, and a condyloma. Also they have cultivated a morphologically identical bacillus from the blood of two syphilitic patients, and in three instances from syphilitic tissues.

The organism is rod-shaped, of variable length, with rounded, sometimes club-shaped ends. The rods are generally beaded, showing 3 to 8 deeply stained segments with uncolored intervals. The bacilli were very numerous in the connective tissue spaces, sometimes in the cells, of all the morbid products mentioned above. Staining by Lustgarten's methods did not show them. Cultivations were made on blood-serum, and produced a thin faintly yellow or brownish yellow layer on the surface of the medium.

The authors have compared this organism with the smegma bacillus, and believe it to be different. Inoculative experiments, as might be expected, did not succeed, since inoculation from syphilitic sores was equally unsuccessful.[1]

Bacillus of Rhinoscleroma.—An organism was first observed in this rare disease by Frisch some years ago. It has been studied by Cornil, Alvarez, and others, and more recently successful cultivations were made by Paltauf and Von Eiselsberg. I have examined the only case which has ever been observed in this country, and the bacilli which were found are figured in the frontispiece (Fig. 1). They appear in two forms: that of slender slightly curved rods, and of shorter ovoid rods with rounded ends. The latter are strongly colored at the ends, but not in the middle. These might seem to be two species, but by transitional forms I am led to believe that the one changes into the other, and probably swelling up and shortening of the rods is a process preparatory to spore-formation. Cornil and Alvarez describe a capsule around the rods, which is not shown by the method of staining here adopted, though I do not deny its existence. The situation of the bacilli has been referred exclusively to cells or to lymphatics and tissue spaces. It seems to me that they occur in all three situations as shown in the figure. No cultivations were made from this case, but in those of German observers the organism was found to grow easily on the surface of gelatine and agar-agar, producing short bacilli, twice or three times as long as they are broad, with rounded ends, and surrounded by a capsule, but sometimes growing out into threads. Inoculated into animals they produced some inflammation, but no lesion like the original disease.

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[1] Lancet, April 10, 1886.

Is is suggested that this organism is like and possibly identical with Friedländer's pneumonia coccus: but the latter is not stained by Gram's method, which I find to color the rhino-scleroma organism perfectly. There is considerable probability that this bacillus is pathogenic in rhino-scleroma; but the peculiar character of the disease excludes the likelihood of ever reproducing it in animals, and thus furnishing absolute proof.

Bacillus Malariæ.—A bacillus supposed to be the cause of ague was found by Klebs and Tomassi-Crudeli in the soil of the Roman Campagna, and was cultivated on gelatine. It forms rods from 2 to 7 μ in length, and also grows out into long filaments of leptothrix. It produces internal spores and requires oxygen for its growth (aërobic). It has, therefore, much resemblance to the hay-bacillus and other allied forms. The connection of this bacillus with disease is not at all proved. When inoculated into animals it produces certain febrile symptoms, but nothing definitely like ague.

Saprophytic Bacilli occurring in Diseased Conditions.

Bacillus Neapolitanus.—This was discovered by Emmerich in the tissues and intestinal contents of cholera patients at Naples, but it is not generally thought to have anything to do with the causation of the disease. It has not been constantly found in cholera, but has been found in the normal intestinal contents, and in putrid fluids. It much resembles the typhoid bacillus in size and shape. A remarkable fact concerning this bacillus is that when introduced in considerable quantity into animals it produces a condition of the small intestine much resembling that of human cholera.

Bacillus of Septicæmia in Man.—Klein has described minute bacilli occurring in the bloodvessels of the swollen lymphatic glands from cases of human septicæma. Their length is from 1 to 2.5 μ, their thickness 0.03 to 0.05 μ. Their pathogenic action has not been studied.

Bacillus Pyogenes Fœtidus.—An organism isolated by Passet from an abscess in the human subject. It was cultivated and when injected into animals was found to cause fatal disease.

Bacillus Saprogenes is the name given by Rosenbach to three bacilli isolated from human products, viz., from plugs of decomposed matter in the tonsils, from fetid perspiration of the feet, and from fetid pus respectively, which are distinguished at I, II, III. All of them in cultivation furnish fetid products, and the two latter were found to produce inflammation in animals.

Pathogenic Bacilli of Animals.

Bacillus of Swine Typhoid.—This is an infectious and destructive disease of swine, in which Dr. Klein (" Reports of Local Government Board, 1877–8 ") discovered that the organs contained a form of bacterium in morphological respects identical with Bacillus subtilis, i.e., consisting of longer or shorter motile rods capable of forming spores. Artificial cultivations of this bacillus reproduced the disease when inoculated into pigs, as well as in mice and rabbits. Pasteur has described a micrococcus from the same disease, while Schütz and others in Germany described a much smaller bacillus than Klein's (measuring 0.6 to 1.8 μ in length, while Klein's is 2 to 3 μ) ; that is, supposing that the German disease is the same as that known in this country.

Bacillus Tetani.—Reasons have already been given for regarding tetanus as a specific disease, and probably produced by a microörganism (p. 352). The bacillus called that of tetanus was obtained by Nicolaier from garden mould. It forms very slender rods, somewhat longer than, but not so thick as, Koch's bacillus of septicæmia in mice, described below. It appears to be very widely spread in various kinds of earth, but not in fecal matters. The cultivation inoculated into rabbits and mice produced the same disease as inoculation of earth; and the bacilli were in two cases found in the spinal cord—once in the nerves near the point of inoculation. Rosenbach has succeeded in producing in animals an inoculable tetanoid disease transmissible through several generations by inserting subcutaneously portions of skin from a man suffering from tetanus subsequent to gangrene. In the original material a bacillus was found similar to Nicolaier's tetanus-bacillus, and the same was found twice in the spinal cord of rabbits, in which the experimental tetanus had been produced. Rosenbach concludes that there is a bacillus of human tetanus identical with that produced from earth, The bacillus is thought to produce its effect by generating a peculiar toxine.

Bacillus of Ulcerative Stomatitis.—Lingard and Batt described in 1883 a peculiar bacillus as occurring in an ulcerative disease of the tongue and buccal mucous membrane of the calf. The bacilli were large, measuring 4 to 8 μ or more, and often grew out into filaments of much greater length. This organism has some bearing upon human pathology, because Lingard found it also in a case of noma, or gangrene in the human subject (p. 140).

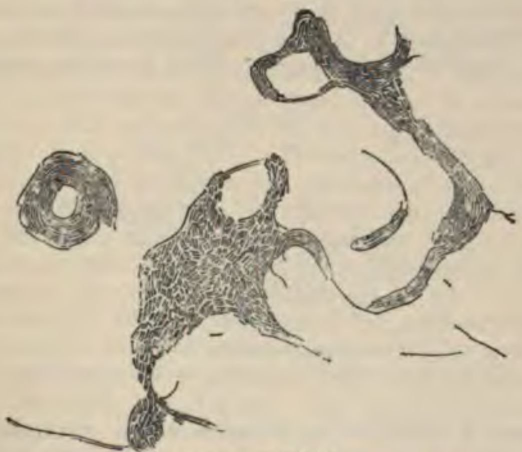
Bacillus of Septicæmia in Mice.—This organism was one of the first obtained by Koch as the result of injecting putrid fluids into mice. He found that by injecting under the skin a very small quantity of putrid blood or other fetid fluids a disease was produced which could be inoculated from one animal to another, and was carried by Koch through fifty-four mice. The blood of the animals showed in every part an extremely minute bacillus, measuring 0.8 to 0.1 μ long, and 0.1 to 0.2 μ thick. It has been cultivated and forms spores. It is remarkable that though fatal to house-mice this bacillus does not affect field-mice.

Bacillus of Symptomatic Anthrax (in cattle).—The disease known by this awkward name is also called "Black Leg" and "Quarter Evil," and in German "Rausch Brand." It causes hemorrhagic swellings in cattle with a fatal termination. The organism producing it has the form previously described as a clostridium, since it produces a single spore at one end, and thus assumes a sort of drum-stick shape (see Clostridium butyricum, Fig. 127). The rods are large, 10 to 15 μ long and 2 μ thick and motile. Spores are formed while the bacillus is still within the tissues or fluids of the animal affected. It has been cultivated, and the cultivations have been found to convey the disease to cattle, sheep, goats, and some other animals; but certain species, such as dogs, cats, rabbits, and others, are immune.

Putrefactive or Zymogenic Bacteria.

Among the merely putrefactive rod-shaped organism one remarkable pleomorphic form may be mentioned.

FIG. 146.



Proteus mirabilis.

Proteus vulgaris has been isolated by Hauser from putrid animal substances along with two other species—P. mirabilis and P. Zenkeri, which need not be specially described.

It forms rods about 0.6 μ thick and very variable in length, sometimes very short or nearly spherical, sometimes like bacilli, sometimes very long threads in a leptothrix form. They are very motile and furnished with cilia. On cultivation this organism shows very remarkable characters. It rapidly liquefies gelatine at ordinary temperatures, producing shallow pits in which are seen the grayish colonies. These send out processes in various directions which show constant movements, and at length some of them become detached and move over the surface of the gelatine-like floating islands. They often show rotary movements. The surface of the gelatine becomes gradually covered with moving colonies.

In addition to these superficial forms, true zooglœa-masses also are produced below the surface of the medium, and the bacterium is capable of passing into *involution forms* or spherical and club-shaped masses, which might easily be mistaken for very different organisms.

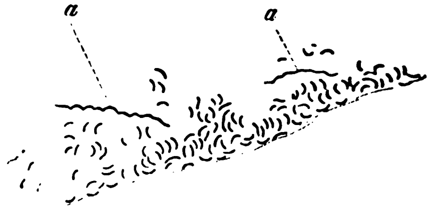
The decomposition of gelatine by these species produces a fetid odor, and they are capable also of decomposing albumen. They are regarded by Hauser as the chief agents in the putrefaction of proteid substances.

Bacterium termo, formerly regarded as the chief putrefactive bacterium, is now a name of somewhat uncertain significance, as several species appear to come under the definition of this species. But the supposed different species have not been isolated.

PATHOGENIC SPIRILLA.

Spirillum Choleræ Asiaticæ: Comma-bacillus.—This organism, first found by Koch in the intestines of persons affected with Asiatic cholera, is seen in the form of curved rods, one-half or two-thirds the length of tubercle-bacilli, varying from 0.8 to 2 μ, the thickness being one-third to one-sixth of the length. They are often joined together

FIG. 147.

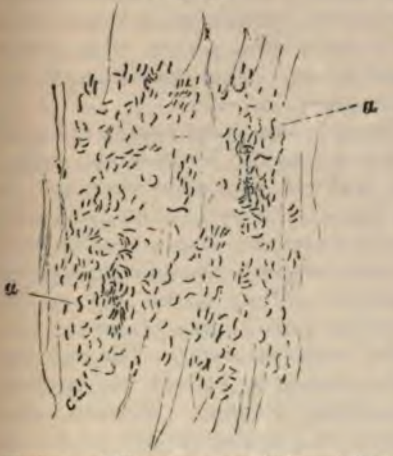


Cholera-spirilla (after KOCH).
From a drop cultivation. *a*, long screw-shaped threads.

so as to make a longer curve or an S-shape. Sometimes a larger number of elements are united together so as to form a long, screw-shaped thread or spirillum, which may consist of ten to thirty turns. Hence the perfect form of the organism is considered to be a spirillum. In drop cultivations the bacilli are seen to be motile, having a rotatory and forward motion.

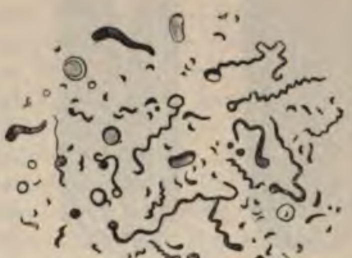
The bacilli multiply rapidly. No spore-formation has been certainly made out, but Hueppe has observed certain spherical bodies formed by the swelling up of a portion of the bacillus, not within it, which he believes to be "Arthrospores." There is, however, no evidence of these being a more permanent form or "resting spores," since Koch has found that if fluids containing bacilli, or linen impregnated with them, once become quite dry, they furnish no bacilli capable of development. The chief variations of form are seen in Fig. 148.

FIG. 148.



Cholera-spirilla grown on moist linen (after KOCH). × 600. Cultivated from the dejections for two days.

FIG 149



Involution forms of cholera-spirilla (after VAN ERMENGEN). × 700.

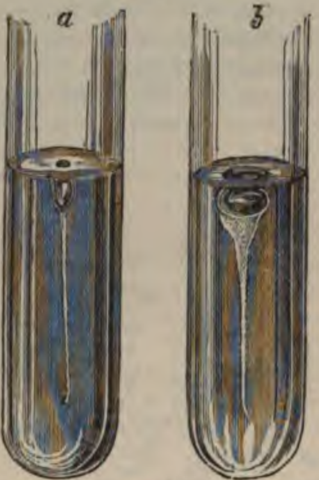
Involution Forms.—When growth in any medium has gone on up to nearly the limit of nutrition certain forms appear which are regarded as indicating involution or regressive change in the bacilli.

The protoplasm becomes irregularly distributed, so that certain portions remain uncolored by the aniline dyes, but not so as to indicate spore-formation. The rods also grow out into club-shaped extremities, or form spherical bodies (Fig. 149). These peculiar forms have been especially studied by Van Ermengen, and are of some importance because their peculiar appearance has in some cases led to their being regarded as belonging to a different organism. Similar involution forms are known to exist in the case of some other bacilli, most strikingly in the case of Proteus already mentioned.

Cultivation of the Cholera-spirillum.—In plate-cultivations on gelatine it forms after twenty-four hours minute circular specks, which as they enlarge become of a yellowish color and granular appearance, looking like little bits of glass; they liquefy the gelatine after forty-eight hours in a funnel-shaped form. A delicate pinkish color is, according to Eisenberg, sometimes produced. If inserted into gelatine tubes it produces, after one or two days, a cloudiness along the track of the needle, with slight liquefaction; but in the upper part of the track the gelatine is liquefied in the form of a funnel, which, containing some air, produces the appearance of a bubble.

The liquefaction extends till, after a week or two, it involves the greater part of the tube, and in a month the contents are liquefied.

FIG. 150.



Tube-cultivations of cholera-spirilla (FLÜGGE.)
a, after two days. *b*, after four days.

On agar-agar the growth is not characteristic. On potatoes "light grayish-brown colonies" are produced which soften into a slimy layer, but growth takes place only at rather high temperatures. On moist linen, kept under a bell-jar to prevent evaporation, the organism grows remarkably well; and a small portion of choleraic stools will in some cases furnish an almost pure cultivation.

The spirillum grows readily in liquid media, as broth, blood-serum, milk; and produces no visible alteration in the latter. In very dilute solutions growth ceases, and this is also the case in water, even when containing organic impurities. But growth may apparently take place in the scum on the surface of very foul water. The nutrient media must never be acid, but are best even faintly alkaline. No fetid odor or gases of putrefaction are produced, but a faint sweetish odor is given off. No growth takes place with absolute privation of air. The optimum temperature is from 86° to 104° F.; on gelatine 72° to 77°. Growth ceases below 60°. A temperature of 14° F. may be borne without perishing.

Cultivations are at once killed by drying up, and may also be extinguished by the competitive growth of other microörganisms, such as putrefactive bacteria, a point which may be of practical importance. It may be also well to note that while the bacilli do not *multiply* in pure water they live in it for a considerable time, and have been found still capable of growth after seven months in natural water previously sterilized, and after ten weeks in sterilized distilled water. The best dyes are a watery solution of fuchsine or strong solution of methylene blue—the latter especially for sections.

The above-mentioned cultivation characters are important as distinguishing Koch's cholera comma-bacillus from other comma-bacilli which agree with it in shape and size.

Cholera-red.—A chemical test has been proposed for cultivations of the cholera-spirillum, namely, the production of a deep purplish-red color on adding nitric or sulphuric acid to them, as observed by Poehl and Bujwid. According to Salkowski, this color depends upon a well-known reaction of nitric (or nitrous) acid with indol, which is one of the products of decomposition of proteid matters. Hence decomposing albumen or fibrin might under other circumstances give the same. But there is a peculiarity in the cultivations of the spirillum that they give the color with pure sulphuric acid; a fact which Salkowski explains by the presence of nitrous acid or nitrites in the cultivations. A red color produced in cholera-stools by nitric acid was noticed many years ago by Simon, Heller, and Virchow.[1]

Occurrence of Comma bacilli.—An organism corresponding both morphologically and in mode of growth to that above described was first observed by Koch in cases of Asiatic cholera, and has since been found with singular uniformity in the intestinal discharges and intestinal contents after death from cases of the same disease occurring both in India and in Europe. Drs. Klein and Gibbes found it very generally in the rice-water evacuations of cholera patients, though sometimes in such small numbers as to be discovered with difficulty by simple inspection. In plate-cultivations they generally appeared along with other microörganisms. They were seen also in the majority of cases in the intestinal contents after death. The same fact as regards the intestinal contents before or after death has been virtually confirmed by all subsequent observers; in India itself by Cunningham and others; in Paris by Van Ermengen and Watson Cheyne, besides several French pathologists: at Toulon by MM. Straus and Roux, who had previously failed to find comma-bacilli in Egypt; at Marseilles invariably by Nicati and Rietsch: in various cities of Italy—Padua, Bologna, Genoa, Turin, Naples, Palermo—by pathologists, native and foreign; in Spain, though not quite so constantly, by Roy and Sherrington. These observations were made in the European epidemic of 1885, and in the next year a local epidemic of cholera in Germany (at Finthen) furnished identical results

Relation of Spirilla to Tissues.—Koch's first observation in India led him to conclude that the spirillum was often present in the walls of the intestine as well as in its contents; but further observations have only partially confirmed this conclusion, the organisms being comparatively rarely found in tissues. Klein and Gibbes could not detect them at all in this situation, other observers only in some cases; Roy and Sherrington found them in very few sections of the intestines, even from severe cases. Since the epithelium of the small intestine is to a very large extent shed off in cholera, the presence or absence of the organism in the actual mucous layer could not be determined. The frequent occurrence of the spirilla in desquamated flakes of epithelium (as in Fig. 151) is not conclusive, since they might perhaps have penetrated these masses after their separation from the walls.

On the whole, it may be taken as proved that the presence of the organisms in the intestinal walls is an occasional, not a constant, occurrence.

In the blood and in internal organs they are more constantly absent, though some observers have found that they are able to penetrate into the blood and organs, such as liver and kidney, in the "guinea-pig cholera" produced by experiment. Moreover, it has been found that the cholera-spirilla if injected into the blood of animals soon die, and are eliminated either by the bowels or otherwise.

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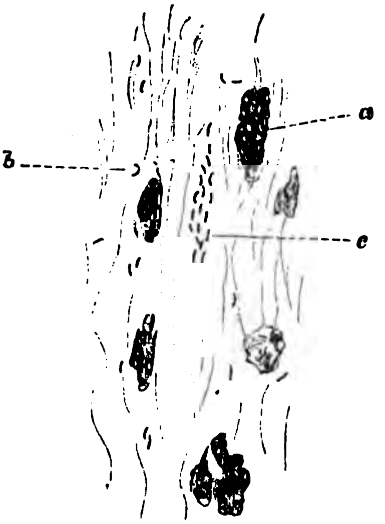
[1] Virchow, Gesammelte Abhandlungen, 1856, p. 101.

In all situations cultivation has proved a surer means of recognizing Koch's organism than simple observation, and the two methods combined have furnished such an enormous mass of evidence in favor of the constant occurrence of Koch's comma under the circumstances mentioned that the comparatively few negative instances may be disregarded.

FIG. 151.



Preparation from intestinal contents (KOCH). × 600.
a, nuclei of necrotic epithelium; *b*, *c*, comma-bacilli.

The next question is whether this spirillum is met with elsewhere than in choleraic intestines, and this question must be answered broadly in the negative. Organisms of similar form have been found in several situations, but with one or two exceptions, to be mentioned immediately, they have on cultivation turned out to be different species. The most striking case is that of the spirillum of "cholera nostras," discovered by Finkler and Prior (spoken of further on), which gives distinct characters on cultivation. A comma-bacillus from the mouth described by the late Dr. Lewis is not cultivable by the same means as Koch's spirillum. It is said that organisms of similar shape are found in the intestines of healthy guinea-pigs, and in the intestinal discharges of healthy persons, or of those suffering from diarrhœa, all of which on cultivation turn out to be different from the cholera-spirillum. The only exception is that Koch has recorded the occurrence of his comma-bacillus in a tank in Calcutta, near which cholera cases occurred; while Klein and Gibbes affirm that they found commas in several tanks, quite unconnected with any question of cholera (and cultivated them by Koch's method); while

Cunningham has found similar organisms on water-plants in India which on cultivation agreed with Koch's comma-bacillus. Others claim to have found organisms similar in form in many natural waters. Putting aside the occurrence of these organisms in water, the explanation of which requires further study, it appears that the cholera-spirillum is never found associated with *any other disease.*

Is there any other organism of which the same may be said? Several, or indeed many, other organisms occur in the choleraic intestine, but no other has been found constantly by all observers; and no other is exclusively coincident with cholera, the Naples bacillus of Emmerich, and a straight bacillus described by Klein and Gibbes, not having been found universally and exclusively.

It seems, then, impossible to resist the conclusion that the positive recognition of a spirillum with the characters above given is *a diagnostic sign of the presence of cholera.*

To argue from the absence of the spirillum to the absence of cholera would be less rigidly accurate on account of the possibility of accident or mistake; but negative results in a series of cases, tested by competent experimenters, would be a fact of great significance. On this ground the methods for the cultivation of the cholera-spirillum, on which its diagnosis really depends, have an obvious importance.

Is the Spirillum the Cause of Cholera?—This question, which is answered in the affirmative by Koch, Virchow, and most Continental observers, and in the negative by Pettenkofer, Klein, and several pathologists in this country of the opposite school, requires some consideration.

One of the conditions laid down by Koch for the proof of a micro-organism being the cause of a disease is that the organism should be passed into the body of another animal, there reproduce the disease, and be found in its tissues and organs.

It is obviously very difficult to satisfy this condition in the case of a disease which does not affect any other animal than man, as is the fact with regard to cholera.

Notwithstanding this objection, numerous attempts have been made to convey the disease to animals. Many species, such as monkeys, pigs, dogs, cats, etc., have been fed with choleraic discharges, but without effect. The same experiments have been tried with cultivations of the cholera-spirillum with an equally negative result as regards disease, but establishing this remarkable fact that these organisms are always killed in traversing the stomach, apparently by the acidity of the gastric juice. Results equally negative followed the injection of choleraic matters, blood, or cultivations into the subcutaneous tissue or blood of various animals, except that in the latter case septicæmia resulted.

Van Ermengen, considering that the seat of the disease was in the small intestine, injected small quantities of a cultivation of spirilla direct into the duodenum of guinea-pigs, and similar experiments were made by Nicati and Rietsch, and other pathologists. The result was that the animals died, and with symptoms somewhat resembling those of cholera, viz., copious transudation into the bowels, with, in some cases, diarrhœa, and constantly, algidity and prostration. The autopsy showed the bowels injected, filled with colorless mucus without fecal odor, just as in human cholera, and containing enormous numbers of the spirillum. This disease could be transmitted through a series of animals by successive inoculations. The organisms were occasionally found in the blood. Similar operations practised with cultivations of other bacilli had no effect. However, the serious character of the operation and the possibility of septicæmia threw some doubt on these results, so that Koch and others have devised means of introducing the spirilla into the intestine without wounding it. Koch introduced into the stomach of a guinea-pig a solution of carbonate of soda enough to keep the contents alkaline for three hours, then, by means of a catheter, broth containing cultivations of the spirillum, and injected into the peritoneum some tincture of opium; which had the effect of checking the peristaltic action of the bowels. On the third day the animals fell ill, and mostly died with the symptoms and post-mortem signs above mentioned. Koch states, however, that cultivations of other similar spirilla, *e. g.*, that of Finkler and Prior, produced similar though less violent effects. Hueppe has lately obtained the same results in a still simpler way by injecting extremely small quantities of spirilla into the peritoneum of guinea-pigs; and Doyen, in Paris, who had experimented on a very large number of animals, sets up the choleraic disease by introducing alcohol into the stomach along with the organisms, thus making no wound at all, and giving no alkali. Moreover, in less rapidly fatal cases true cholera, *i. e.*, diarrhœa, accompanied by "rice water" dejections was caused. It is said that diarrhœa from other causes is an almost unknown disease in guinea-pigs.

There can be no doubt that the "guinea-pig cholera" thus set up is a definite disease, always associated with the presence of cholera-spirilla in the intestines, and, as may fairly be concluded, caused by these organisms. Its likeness to human cholera is perhaps as close as might be expected, though it falls short of identity, and the analogical argument that human cholera also is caused by the spirilla is a very strong one, though this also seems to fall a little short of actual demonstration. Koch's explanation of the facts of cholera is that the spirillum, being received into the digestive canal, multiplies there and generates a poison which produces the symptoms of the disease. It must further be supposed that there is some influence, such as previously existing in catarrh, which modifies the acidity of the stomach, so as to permit the bacilli to pass—and possibly of the intestines, favoring their settlement there.

Is there a Cholera Poison?—If cholera is produced by any organism living in the intestine, which does not enter the blood, it can only be by means of some poison generated in the bowels and absorbed. If there is any such absorption, it must have already taken place when the first symptoms appear, especially as after this the whole intestinal tract is in a condition which makes absorption virtually impossible.

the existence of such a poison is highly probable on grounds of analogy, and equally so whether we assume the organism producing it to live in the human intestine or in the outside world; but attempts to discover it have at present led to no specific results. The products of decomposition of nutrient media by the comma-bacillus have not been found to differ essentially from those generated by putrefactive bacteria, consisting of ptomaïnes and toxines such as have been already spoken of.

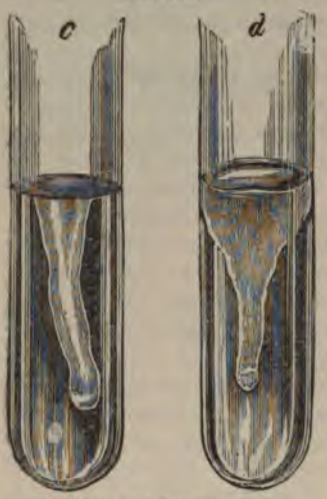
Is the Cause of Cholera Something External to the Body?—Some hold that the phenomena of cholera cannot be explained by any cause acting within the human body, but that the real infecting or poisoning agent must be in the soil. As was pointed out before, this does not exclude the possibility of the virus being conveyed from one country to another by human beings, or even under certain circumstances by dead objects. It is only necessary to consider for a moment how this bears on the bacterial theory of the disease. The cholera-spirillum may be conceived of as preserving its vitality in damp soil or water (and even multiplying, if there be sufficient organic matter to supply it with nutriment), but it will not bear drying. The range of temperature within which it can grow corresponds to summer heat in temperate climates, and that of all seasons in the tropics. On the whole, there is nothing to make it impossible that the organism should live for a time in the human body and for a time outside, and in each phase of life generate a poison. The supposition of a poison generated by the organism in the soil or in water and received into the human body would explain only part of the facts, though it is not inconceivable that this may be the explanation of some suddenly fatal cases of cholera, that is, they are *poisonings*, not *infections*. But it is necessary that there should be an infection also in order that the virus may be carried further and may continue to live.

Conclusion.—It is impossible to enter further upon the very interesting questions connected with cholera. The above brief and fragmentary statements of facts must be left to point their own moral. But, on the whole, we may conclude that the conditions formerly stated as necessary for the cause of cholera, that it should be a living organism having the power of generating a specific poison, are to a large extent met by the hypothesis of the cholera-spirillum being that cause. Still more must be known about the independent or ectogenic life of the spirillum before it can be said to account for the local or miasmatic facts of cholera, which are quite as important as those which relate to its being a communicable infective disease.

As a biological analogy, it may be pointed out that the cause of cholera being in all probability aquatic, might be expected to belong to the group of spirilliform bacteria which spend their life in water or fluids, just as the anthrax-bacillus might be expected to be allied to the bacteria belonging to grass or other vegetable food of the animals which it attacks.

Spirillum Finkleri.—This organism was discovered by Finkler and Prior in the dejections and intestinal contents of cases of "cholera nostras," or what we call English cholera. It was at first thought to be the same as Koch's comma-bacillus, but can be distinguished by certain characters in cultivation, and to some extent by form. It produces curved rods which are occasionally united into **S** figures and spirals. They are said to be slightly longer and thicker than Koch's commas, and more pointed at the ends.

Fig. 152.



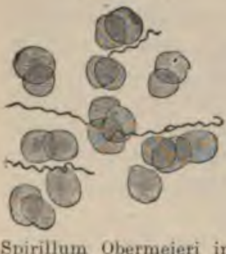
Finkler's and Prior's comma-bacillus.
Cultivations in gelatine. *c*, two days old. *d*, four days old.

But the main distinction between the two species is brought out by cultivation.

In plate-cultivations Finkler and Prior's bacillus forms round colonies which are more sharply defined than Koch's, and have not the wavy outline which the others have. When inserted into tubes of gelatine the organisms now spoken of liquefy the gelatine with much greater energy than Koch's, and do so all along the track of the needle, not only at the top, so that a very different appearance is produced, as seen in the figure. There are also peculiarities of growth on other media. It is also noticeable that cultivations of Finkler's bacillus produce a disagreeable fetid odor, quite different from that of the cultivations of Koch's.

This organism has been introduced into guinea-pigs and disease has resulted—fatal in thirty per cent. of the cases. The same mortality was obtained by Koch in experiments conducted in the same way as those with the cholera-bacillus.

Fig. 153.



Spirillum Obermeieri in blood (Flügge). × 500.

It must remain doubtful whether in man it produces any pathogenic effect, and most observers have failed to find it in cases of European cholera.

A spirillum or comma-bacillus obtained by Deneke from old cheese much resembles Finkler and Prior's, and also Koch's spirilla, but is distinguished by its characters on cultivation.

Spirillum Obermeieri was discovered in the blood of patients suffering from relapsing fever. It forms long, wavy, flexible threads in spirals of from ten to twenty turns, measuring sixteen to forty inches in length and extremely thin.

The threads are highly motile and, according to Koch, are furnished with cilia. No spores are known.

The organism is found in the blood only, not the tissues; but is constantly present during the febrile paroxysms, not in the intervals of the fever, except for a day or two. It has never been successfully cultivated.

If blood from a case of the fever be injected into monkeys under the skin, a fever is produced in them, during which the blood contains numerous spirilla; but when it subsides the spirilla again disappear.

The fever in monkeys does not show the typical relapse of the human disease. The blood of the affected monkey may be used to give the fever to others by inoculation. One attack gives no immunity.

As it is not known how the organism enters the body or how it leaves it, if at all, its natural history may be said to be unknown. But, considering its constant occurrence and the possibility of transmission by inoculation, it seems impossible to doubt that it is the cause of the disease.

APPENDIX.

METHODS FOR EXAMINATION AND RECOGNITION OF BACTERIA.

WITHOUT entering into minute technical details, a few words must be said about the methods of recognizing and preparing specimens of bacteria.

For all examinations of these organisms good microscopes and high powers are essential. It is true that many species may be just seen with moderate powers, such as 300 diameters, but for any proper study of them a power of at least 600 diameters is necessary. The homogeneous or "oil immersion" objectives constructed on Mr. J. W. Stephenson's principle by Professor Abbé and Herr Zeiss, of Jena, and now to be had of most makers, British and foreign, possess great advantages over any others. Another important optical aid is a good condenser such as that of Abbé; and the special method of using it recommended by Koch is the best for showing stained bacteria, though not for other purposes. The condenser is to be brought close up to the object; no diaphragm or a very wide one used, and a plane mirror. The objects are best seen in a medium the refractive power of which is equal to glass, and Canada balsam dissolved in xylol or turpentine is generally used for permanent preparations. For temporary purposes, cedar oil as used for the objective, does quite as well; and the objects may be viewed in glycerine or even in water, but the former is not to be employed for permanent preparations.

The thinnest procurable cover-glasses should always be made use of.

Preparation of Objects.—In examining secretions or other fluids for bacteria, the mucus, blood, or whatever it may be, is dried on cover-glasses in the thinnest possible film, obtained by pressing two cover-glasses together. In certain cases these films are heated to cause them to adhere more firmly to the glass during the subsequent processes. Sections of tissues are made by the ordinary methods, but a microtome must be regarded as essential. For hardening alcohol is generally used; though Müller's fluid and chromic acid are quite admissible. Fresh tissues are usually placed at once in absolute alcohol; and only very small pieces (say a quarter of an inch thick) must be used. This prevents any possibility of putrefaction, and thus gives security against error; but it is not always the best plan to show the structure of tissues.

To exhibit the bacteria in mixed objects or tissues, the method formerly used was to make all other parts transparent with solution of potassa or soda, the microörganisms remaining as brilliant objects. A much more satisfactory plan, however, is to stain them with some dye, which they absorb either exclusively or more powerfully than the other objects, thus becoming conspicuous.

Staining Bacteria.—The remarkable affinity of bacteria for coloring matters, and especially for the aniline dyes, much facilitates their recognition, so that the discovery by Perkins in 1856 of the first aniline color has been indirectly of great service to pathology. These colors were introduced for staining bacteria by Weigert in 1871. Out of the many colors used the following are sufficient for almost every purpose: *Fuchsine* or magenta, properly called hydrochlorate of rosaniline; *methyl-violet*, or a variety called *gentian-violet; methylene-blue*, and a red color not made from aniline called *eosine*. The latter is used to stain not the bacteria, but other parts, in order to produce a contrast of color. *Bismarck-brown* is sometimes used for the same purpose.

These colors may be kept dry, or, more conveniently, in saturated alcoholic solutions, except eosine, which is best dissolved in water.

For use they are always greatly diluted, and some formulæ for dilute solutions will now be given. All solutions should be filtered immediately before use.

Methylene-blue is best used in Löffler's solution, called by its inventor a universal reagent, and in my experience the most generally applicable of all. It colors moulds as well as bacteria. To make it, take alcoholic solution of methylene-blue 166 parts by measure (or say eleven drachms), liquor potassæ (B.P.) one part (say four drops), distilled water 554 parts (say enough to make six fluid ounces).

Koch uses a much weaker solution, containing only one part of methylene blue solution in 200 water; and twice as much alkali as Löffler's solution.

Preparations are soaked for a few minutes, or in the case of sections, some hours in these solutions, and afterward dipped in water containing half per cent. of acetic acid; then washed in alcohol, but not too much.

Methyl-violet is a powerful purple dye. Gentian-violet is merely a manufacturer's variety of the same, which possesses no advantages and appears to me to be inferior to what is sold as methyl-violet; an experience confirmed by others. It may be employed in the following methods:

(1) Dilute solutions may be made by adding five or six drops of concentrated solution to a watch-glass of distilled water.

(2) It acts more powerfully if diluted with aniline water. This is made by shaking up aniline oil with distilled water to saturation, allowing to stand for five minutes in a warm place, and filtering. The concentrated solution of the dye is then added drop by drop, till the fluid becomes opalescent (Ehrlich).

(3) Weigert's solution is made as follows: Concentrated solution of methyl-violet, 11 parts (or one drachm); aniline water, 100 parts (or nine drachms); absolute alcohol, 10 parts (or one drachm).

(4) Where the solution is used rapidly it will do to put an excess of the solid dye into a bottle with aniline water, to which one-tenth part of alcohol is added, and allow the solution to become saturated, filling up with alcohol and aniline water from time to time as required.

The addition of aniline to the solutions makes their coloring more powerful, and also more permanent.

Fuchsine.—Solutions of this red dye may be made in the four methods described for methyl-violet.

In addition, a carbolic solution (Neelsen's) is used, which is prepared as follows: Make a solution of carbolic acid in distilled water in the proportion of five per cent., and add one-tenth part of a concentrated solution of fuchsine. Otherwise, thus: fuchsine one part (by weight); absolute alcohol 10 parts; five per cent. solution of carbolic acid 100 parts.

The solution keeps much better than the aniline solutions, and carbolic acid has the same action that aniline has in increasing the coloring power of the dyes.

The above are the colors chiefly used for staining bacteria, but in order to display the tissues or cells it is often desirable to stain them of some contrast color. If the bacteria are colored red, then methylene blue in dilute solution may be used as a contrast stain. If they are blue, eosine in a one or two per cent. watery solution, or a solution of carmine or picro-carmine may be used. Another color sometimes employed for this purpose is Bismarck-brown in a two per cent. aqueous solution.

The general principle of staining bacteria is to allow the color to act on the whole preparation, and then to extract it from all parts except the bacteria, which retain it with greater tenacity, especially if the color has been combined with aniline. As decolorizing agents we may use first distilled water, which may be sufficient in some cases; then alcohol, which extracts some colors very completely, but may act too strongly. Oil of cloves, and in a less degree turpentine, act as decolorizing agents if used for mounting. By taking advantage of the solvent powers of the above fluids, sufficient decolorization is often effected, but for certain purposes special methods are used, of which some examples will be given.

Gram's method is one of the best for obtaining an isolated staining of bacteria. An aniline water solution of gentian-violet (or, still better, methyl-violet) is prepared, in which preparations are soaked for periods varying from some minutes (cover-classes) to several hours (sections). They are then placed in an iodine solution prepared as follows: Iodine one part, potassium iodide two parts, water 300. In this they remain for from one to three minutes, till they turn brown. They are then placed in alcohol till the brown color is completely washed out, and may be counter-stained with eosine or Bismarck-brown. Oil of cloves may be used if necessary for complete decolorization. This method leaves most bacteria stained purple; but certain portions of tissues, especially the granules of plasma-cells, and sometimes nuclei, will sometimes retain the color. This method is suitable for the microörganisms of suppuration, septic bacteria, the bacilli of tubercle and anthrax and rhinoscleroma, and for anthracomyces. Some others, *e.g.*, the cholera bacillus, that of typhoid fever, the coccus of gonorrhea and Friedländer's pneumo-coccus, are decolorized.

To Examine Sputum for Tubercle Bacilli.—Take a small quantity of the yellowish or opaque part of the sputum (avoiding pure mucus) with a needle, and spread on a perfectly clean cover-glass. Press on this another cover-glass, and squeeze the matter between the two, removing the superfluity from the edges with blotting-paper or rag. Then slide the glasses off one another so as to leave the thinnest possible film upon each. Leave the glasses to dry. When dry, take up with forceps, and pass three times rather slowly through the flame of a spirit lamp or Bunsen's gas burner with the film uppermost, but not so as actually to scorch it.

Then float the cover-glasses with the coated side downward in a watch-glass or saucer containing a solution of fuchsine prepared by Weigert's or by Neelson's method given above.

The solution may be previously heated in a test-tube till bubbles begin to appear, and then poured into the saucer; or the watch-glass may be cautiously heated over the lamp in the same way. This accelerates the process, but is not necessary. The staining is then complete in five or ten minutes. In the cold two or three hours should be allowed, to be quite sure, though half an hour is usually enough.

The red-stained cover-glass is then dipped for a few seconds in dilute nitric acid (concentrated acid, one in three or four) for aniline solutions, or sulphuric acid (one in twenty), if the carbolic solution has been used.

The whole preparation is now colorless, except the tubercle bacilli, which are red. To show the cells and any other bacteria which may be present, stain for a few minutes in dilute solution of methylene-blue, wash in distilled water and allow to dry. When dry, place the cover-glass on a drop of Canada balsam, dissolved in turpentine or xylol, on a slide, and the mounting is complete. The cells, etc., will appear blue, the tubercle bacilli red. Cedar oil is more convenient than balsam for immediate examination; and the cover-glass may afterward be transferred to balsam, if desired.

Other methods are based on the fact that methylene-blue displaces the color of fuchsine in all elements except the tubercle bacillus. Heneage Gibbes's rapid method depends upon this. His double-staining solution is prepared as follows:

Fuchsine	2 parts.
Methylene-blue	1 part.

Triturate in a glass mortar.

Dissolve aniline oil, three parts, in rectified spirit fifteen, and add slowly to the above. Lastly, add slowly, distilled water fifteen parts. It may be obtained ready made in the shops.

To use this solution, heat a little in a test-tube till bubbles of air form; pour into a watch-glass and float the cover-glasses upon it, or immerse them for five minutes. Wash in methylated spirit till no more color comes away; dry and mount in Canada balsam. If the liquid be not heated, an hour is required for staining. The same objects are stained blue and red respectively, as in the other method.

This is the shortest method for clinical purposes, and if a *positive* result is obtained, is perfectly trustworthy, but from my own experience I prefer Neelsen's method. Other secretions, such as pus, urine, etc., may be examined in the same way as sputa.

Staining of Sections is effected on the same principle as that of cover-glass preparations, but the sections require soaking for twelve or twenty-four hours in the original staining solution. Before mounting in balsam, the section should be cleared with turpentine rather than with the clove oil generally used; Koch recommends oil of cedar. But if the sections be deeply stained first, the decolorizing action of clove oil may be made useful. The carbolic solutions (Neelsen's) are not recommended for staining sections.

For sections containing tubercle, Weigert's fuchsine solution is probably the best. For many other purposes Gram's method is the most satisfactory. Contrast stains may be advantageously used with both.

Epidermic Preparations.—Scales or sections of skin are difficult to stain, because all epidermic structures, including hairs, absorb the colors very strongly. The best plan is first to remove all fat from the objects by soaking in ether—for some hours, if necessary—generally a few minutes will suffice. Then add to the scales, on a slide or cover-glass, acetic acid diluted with an equal part of water. Press between two cover-glasses, or two slides placed conically, so that the specimens softened by the acid may be flattened out as much as possible. Then separate the glasses and allow them to dry spontaneously. The microörganisms, whether bacteria or fungi, may now be stained with Löffler's methylene-blue solution, and washed with strong spirit, when the epidermic cells and hair give up most of their color, leaving the organisms colored blue.

The above coloring methods are sufficient for most purposes, though special methods have to be used in certain cases.

Mounting Preparations.—Bacteria stained as above may be examined in glycerine or even water for temporary purposes, but for preservation should be dehydrated with absolute alcohol, and either dried in the air or passed through cedar oil, and mounted in a solution of Canada balsam, best made with xylol. For clinical purposes, examination in cedar oil is generally sufficient, and the glasses are more easily cleaned. Oil of cloves is a somewhat dangerous medium.

For other methods and practical details, reference must be made to special works.

BIBLIOGRAPHY.

THE following list of a few of the numerous publications on the subject may be useful:

General Biology of Bacteria.

The best work accessible to the English reader is:

A. DeBary's "Lectures on Bacteria," translated by H. E. F. Garnsey, and revised by Prof. J. B. Balfour. Oxford, 1887.

The same author's larger work may be also referred to:

"Comparative Morphology and Biology of the Fungi, Mycetozoa and Bacteria." In English by the same translator. Oxford, at the Clarendon Press.

In German the most comprehensive work is:

C. Flügge: "Die Mikroörganismen." Leipzig, 1886.

See, also, W. Zopf: "Die Spaltpilze." Third edition. Breslau, 1884. Is botanical.

Bacteria in Relation to Disease.

Klein: "Microörganisms and Disease." Third edition. London, 1886.

Cornil et Babés: "Les Bactéries et leur rôle dans les maladies infectieuses." Second edition. Paris, 1886.

Baumgarten: "Lehrbuch der pathologischen Mykologie," Braunschweig, 1888 (in progress).

Practical and Technical Works.

E. M. Crookshank: "Manual of Bacteriology," second edition. London, 1887. Numerous plates.

F. Hueppe: "Die Methoden der Bakterien-Forschung," third edition. Wiesbaden, 1886.

F. Hueppe's "The Methods of Bacteriological Investigation," translated by Biggs.

Woodhead and Hare: "Pathological Mycology," Part I. Edinburgh, 1885.

Huber und Becker: "Die pathologisch-histologischen und bacteriogischen Untersuchungsmethoden." Leipzig, 1886.

Special Memoirs.

A very few only can be mentioned here. Numerous references are contained in Dr. Crookshank's work cited above, and since 1885 they are given very completely in Baumgarten's "Jahresbericht über pathogene Mikroörganismen," of which two volumes have appeared, for 1885 and for 1886.

R. Koch, on "Traumatic Infective Diseases," translated by W. Cheyne, New Sydenham Society. London, 1880.

"Recent Essays on Bacteria in Relation to Disease," edited by W. Cheyne, New Sydenham Society. London, 1886.

The Reports of the Medical Officer to the Local Government Board, for
years past, contain numerous memoirs by Klein, Burdon Sanderson, L
Lingard, and others. "Mittheilungen des Reichsgesundheitsamts Berlin.
tain memoirs by Koch and others.

Cholera.

Memoirs by Koch, translated in the Sydenham Society volume on "Ba
Relation to Disease." Also in *British Medical Journal*, 1884, vol. ii.

Inquiry by Drs. Klein and Gibbes, and Transactions of a Committee
by the Secretary of State for India in Council (Blue Book, 1885).

Van Ermengen: "Recherches sur le Microbe du Choléra Asiatique." Pa
Bruxelles, 1885.

Watson Cheyne: "Report on the Cholera Bacillus," *British Medical Jo*
1885, vol. i.

Report of the Second Cholera Conference at Berlin, *British Medical Jou*
1885, vol. i.

See also Report of Discussion at Royal Medical and Chirurgical Society. M
24, 1885, with memoirs by Klein and others, in same volume.

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